INTERNATIONAL RECORD OF MEDICINE

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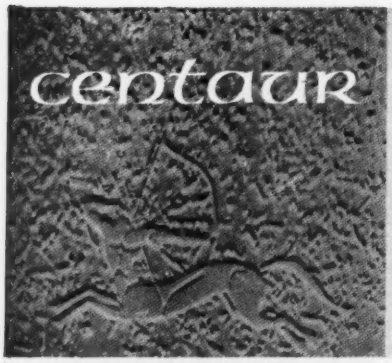

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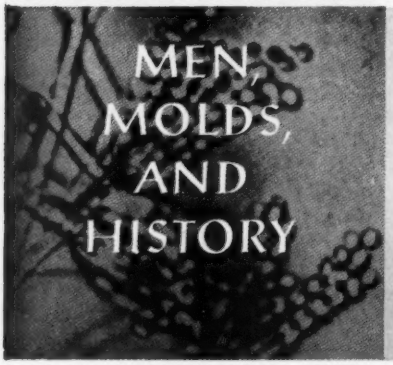

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Pulsed Short Wave in the Treatment of Bursitis with Calcification

Abraham J. Ginsberg, M.D.

NEW YORK, N. Y.

High frequency electrical energy has been employed in the treatment of disease for more than two decades. It has employed many modalities. Most have involved continuous excitation of tissue at energy transfer rates that produce pyrexia, to the extent that heating was long considered to be the source of benefit to patients.

But since 1935 the technique of pulsed short wave therapy, which does not produce pyrexia, has come into increased use. Laboratory findings by Herrick et al,[1] Heller,[2] Erdman,[3] and Bach,[4] together with clinical successes, have rather radically changed our physiological understanding and altered our views toward the syndromes for which short wave therapy is indicated.

I present here clinical data relating to subdeltoid bursitis with associated calcification in 94 patients treated by me over a period of 15 years. In each case pulsed short wave was the sole therapy employed.

Although it is now in mass production, the modality I used was of my own design.

DESCRIPTION OF APPARATUS

Operating on standard 110 volt current, at a frequency of 27.12 megacycles, the machine delivers high intensity energy in short bursts or pulses. Between each burst is a considerable rest period to allow for dissipation of heat. Specifically, a single pulse of energy has a maximum duration of 65 microseconds, whereas the interval between pulses (at maximum setting) is 1665 microseconds. Thus power is transmitted less than 4 per cent of the time.

Even when energy is emitted in the top strength of 1025 watts, the average output, taking the rest periods into account, is but 40 watts. To this extent has the danger of burning been reduced. Nor are there known contraindications. My experience has been that the machine is entirely safe.

The field of energy transmitted through the treatment head is roughly 6 inches in diameter. Depth of penetration into the body is determined by a dial setting. An-

TABLE I

Data on Symptomatic Relief Obtained

No. of patients	Roentgenograms taken	Extent of relief			Total relieved	
		None	Partial	Complete	No.	Percentage
48	Only before treatment	6	4	38	42	87.5
46	Both before and after treatment	2	2	42	44	91.3

TABLE II

Data on Calcium Absorption

No. of patients	Extent of absorption				Total showing absorption	
	None	Some	Marked	Complete	No.	Percentage
46	4	3	15	24	42	91.3

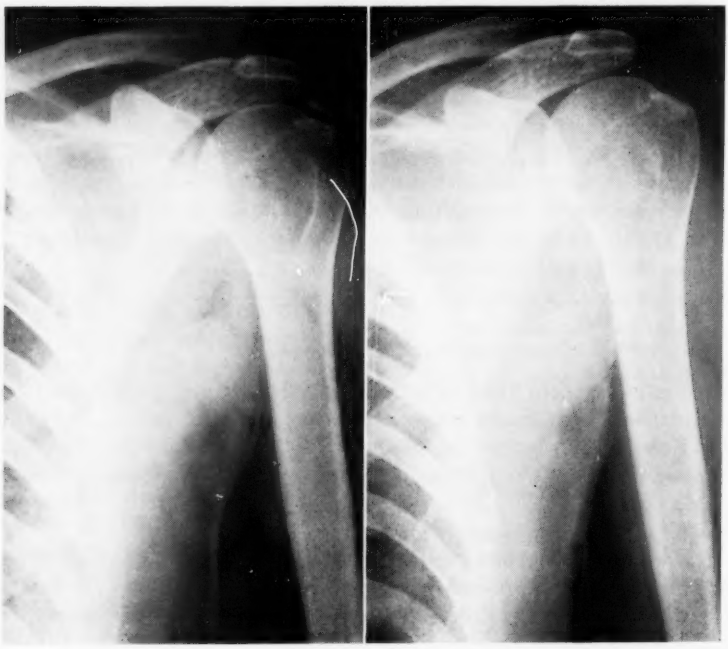

FIG. 1. Roentgenograms taken before (left) and after (right) treatment of Mrs. E. Y., a housewife aged 35. She received 32 treatments from October 11 to January 31. Calcification was completely absorbed.

other dial gives a choice of pulse frequencies: 80, 160, 300, 400, 500, or 600 pulses/second.

TREATMENT TECHNIQUE

The patient sits or lies comfortably beneath the treatment head. There is no need for disrobing. First the affected area is treated for 10 minutes, at 600 pulses/second and maximum setting of 6 on the penetration dial. Thereupon 10 minutes of irradiation, at 400 pulses/second and a setting of 4 on the penetration dial, is directed at the liver and the adrenals.

This latter exposure comes out of my strong conviction, based on long experience, that the main centers of body defense can profit from treatment as much as the affected area.

RESULTS OF TREATMENTS

The presenting symptoms of the 94 bursitis patients varied from mild discomfort to excruciating pain accompanied by limitation of motion. Some patients applied for relief immediately after experiencing the first symptoms, while others reported they had undergone months and even years of intermittent pain. More than half the patients in this study group stated they had received one or more forms of treat-

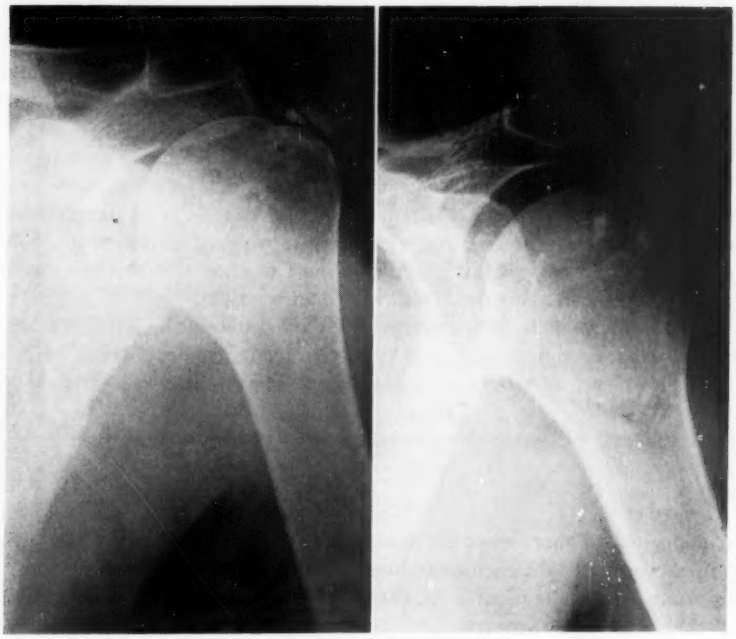

FIG. 2. Roentgenograms taken before (left) and after (right) treatment of Mr. H. L., a broker aged 35. He received 28 treatments in a three-month period. Calcification was completely absorbed.

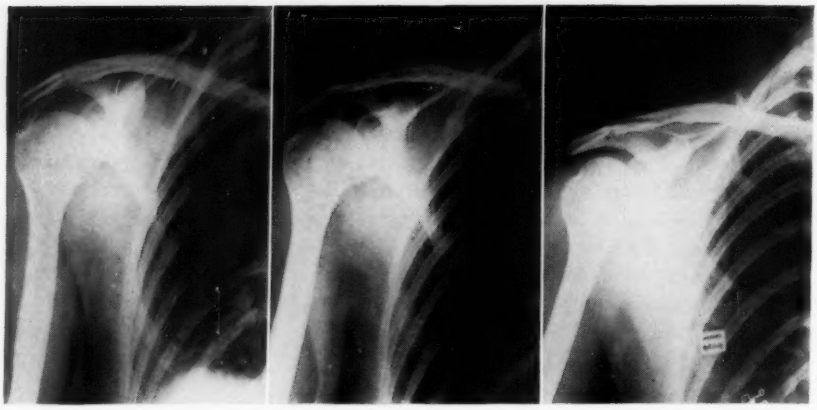

FIG. 3. Roentgenogram (left) taken before treatment of Mrs. E. H., a housewife aged 46. She had had pain for six months before treatment. After eight visits, motion without pain was achieved. There was progressive improvement to complete comfort after 15 visits. She was discharged as cured after 34 visits, although slight evidence of calcification was still present (center). Roentgenogram made one year later showed complete elimination of decalcification (right).

ment from other physicians. These included aspiration of the bursa, diathermy, immobilization, vitamin B injections, local anesthesia, massage, procaine hydrochloride injections, surgery, osteopathic manipulations, and radiological therapy.

By my direction roentgenograms were taken of each patient, prior to treatment, in order to establish the presence of calcium.

Many of the patients had been referred by other physicians, and thus it was not possible to insist that treatment continue after pain and symptoms were relieved. Since the period of treatment that is required to show evidence of complete decalcification is three or four times as long as the period required to restore mobility and comfort, only 46 patients of this group continued treatment to the point at which final roentgenogram showing decalcification could be taken.

Table I summarizes data on the symptomatic relief obtained. Table II shows the number of patients, among those in whom roentgenograms were taken both before and after treatment, in whom calcium absorption was apparent on final roentgenogram.

Figures 1, 2, and 3 illustrate 2 typical cases and 1 protracted case.

SUMMARY

The use of pulsed short wave for treatment of calcified bursitis, without drugs or other therapeutic modalities, has produced impressive clinical results.

This study covers 94 patients. Of these, 86 achieved partial or complete symptomatic relief.

Of 46 patients in whom roentgenograms were taken both before and after treatment, there was observable absorption of calcium in 42 cases.

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Pericarditis in Myocardial Infarction

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That a fibrinous pericarditis with a friction rub may appear shortly after myocardial infarction is widely known. It is not, however, sufficiently appreciated by clinicians that the pain of such pericarditis may be quite severe and prominent. Furthermore, the appearance of the characteristic pain of myocardial ischemia succeeded closely by the equally characteristic pain of pericarditis represents a chain of events almost pathognomonic of myocardial infarction. The two case histories that follow will serve to illustrate these points.

REPORT OF CASES

CASE 1. R. F., a 69-year-old Jewish widow, was first seen on Oct. 14, 1957, at which time she gave a history of hypertension of five years' duration with an initial systolic reading of 250. For two years she had experienced anterior chest pain on exertion, relieved by rest and glyceryl trinitrate. For more than one year attacks of anginal pain had occurred even at rest and occasionally at night. In the previous summer the patient had been able to walk no more than two blocks before pain developed. Six weeks previously she had been seen at home for an episode of paroxysmal nocturnal dyspnea and was treated with mercurials, digoxin, acetazolamide, and low-salt diet. Anginal pain, however, became progressively more prominent. One sister was diabetic and two brothers had died of heart disease in their fifties.

Physical examination revealed an elderly woman with slow tremor of head and arms. The blood pressure was 174/90. Clinical examination of the heart and lungs was not remarkable. There was no evidence of congestive failure. Urinalysis revealed a trace of albumin. The blood sugar was 96 mg./100 ml. Neurological examination disclosed a cogwheel phenomenon. An electrocardiogram revealed widespread S-T depressions characteristic of digitalis effect.

On Nov. 9, 1957, at about 6 P.M. the patient developed severe substernal pain accompanied by a cold sweat. She was seen at home several hours later and was found to be pale and sweaty. The blood pressure had fallen to 110/70 but the heart sounds were good and regular. An electrocardiogram revealed the classical pattern of diaphragmatic wall infarction. Meperidine administration was followed by repeated vomiting. Bishydroxycoumarin was begun and the patient was hospitalized the next day. Chest pain was mild and was controlled by occasional doses of propoxyphene. The blood pressure was 118/70. On November 11 the temperature rose to 101.6 F. The white count was 15,000 with 77 per cent neutrophils and the sedimentation rate was 37 mm./hr. (Westergren). At 9:15 P.M. the resident was called to see the patient because of the occurrence of left shoulder pain. The only finding on examination was the presence of an occasional râle at the right base. Meperidine was required to relieve the pain.

The next morning, November 12, the patient was complaining of pain in the left side of the chest, accentuated by breathing. The blood pressure was 110/60 and crepitant râles were audible up to the angles of the scapulae. The resident was of the opinion that the pain was due to coronary or pleuritic involvement. The temperature was 101 F. On the same day I wrote: "I believe this type of pain is not due to myocardial ischemia or to primary pleuritic pathology. I have observed it frequently after the subsidence of the acute pain of occlusion. It is substernal and thoracic in location and is characteristically accentuated by breathing. I have assumed that the pain may be due to the acute pericarditis of infarction. It usually lasts 12 to 36 hours."

At 8 P.M. on the same day the resident was again summoned to see the patient, who was complaining bitterly of sharp chest pain, aggravated by deep breathing and change in bodily position. There was no radiation, dyspnea, or hemoptysis. Temperature was 99.4 F., blood pressure was 120/60, and pulse was 86. Bilateral crepitant râles were heard posteriorly but no pleural rub. A leathery, pericardial friction rub was heard throughout the precordial area, obscuring the heart sounds. There was marked point tender-

ness in the left fourth intercostal space near the sternum, which was identical with the pain experienced by the patient. On November 13, the rub was no longer audible but there was mild left precordial pain. On November 14 this was replaced by a precordial ache, and on November 15 all pain had vanished, and the temperature was normal. The remainder of the patient's course in the hospital was uneventful except for the appearance of left lower quadrant pain and mild fever on December 5, presumably due to an acute diverticulitis. The electrocardiograms revealed progressive changes as seen in diaphragmatic wall infarction. Roentgenogram of the chest on December 12 disclosed some increased prominence of the hilar vessels, the presence of a small effusion in the right costophrenic sinus, and enlargement of the heart to the left.

CASE 2. J. L., a 65-year-old business executive, was seen in the office for the first time on Feb. 28, 1958. At that time he stated that the presence of diabetes mellitus had been discovered during an insurance examination 1½ years previously. The blood sugar, originally 220 mg./100 ml., had recently been found to be 117 mg./100 ml. The patient was taking 0.5 Gm. of tolbutamide daily. Intermittent claudication had been noted for two to three years. One brother was diabetic. On July 27, 1959, the patient mentioned that he had recently experienced pain in the left arm for an entire day. An electrocardiogram was normal. On Nov. 9, 1959, another electrocardiogram was normal. On Nov. 17, 1959, the patient underwent surgery for a right indirect inguinal hernia without incident.

On the morning of Dec. 6, 1959, the patient was seen at home because he had experienced severe oppression in the anterior chest radiating down the left arm since midnight. He appeared pale, the heart sounds were very poor, and râles were audible at both bases. The blood pressure was 110/80. An electrocardiogram revealed the presence of left bundle branch block. This finding persisted throughout the course of the illness, making the electrocardiogram worthless thenceforth for the diagnosis of infarction. The patient had no further pain that morning and afternoon. He was hospitalized, and treatment with anticoagulants was initiated. That evening he began to complain of mild substernal pain on breathing, and a pericardial rub limited to the apical area was heard. On the morning of December 7 the patient continued to complain of respiratory pain and a loud pericardial rub was audible over the entire precordium. The temperature was 101.6 F. Râles were present at both bases and the blood pressure fell to 84/62. Intravenous levarterenol was started. The white count was 12,900 with 86 per cent neutrophils. The sedimentation rate was 61 mm./hr. (Westergren) and the serum transaminase (SGOT) 94 units/ml. The blood urea nitrogen was 19 mg./100 ml. and blood sugar 288 mg./100 ml. At 5:45 P.M. the rub was still present although less widespread. On December 8 there was less pain on breathing, located in the left posterior shoulder region instead of at the sternal notch. A faint friction rub was still audible. The temperature was 100.6 F. and it was possible to discontinue the levarterenol. On December 9 all pain had disappeared. The last vestige of pericarditic pain was localized to the root of the neck near the origin of the left sternomastoid muscle. The remainder of the patient's month-long stay in the hospital was uneventful. Therapy consisted of bishydroxycoumarin, tolbutamide, and digoxin.

DISCUSSION

With few exceptions, in most of the standard texts on cardiology, pericarditic pain in myocardial infarction is either not mentioned or is alluded to in a very brief manner. Thus no mention of pericardial pain could be found in the clinical description of myocardial infarction in the standard books by Levine,[1] Goldberger,[2] White,[3] and Sigler.[4] Plotz,[5] in his book *Coronary Artery Disease*, made the following astonishing statement: "In my experience, pain cannot be attributed directly to the pericarditis of coronary disease. Pericarditis is probably negligible clinically except as a minor confirmatory sign in the diagnosis." Similarly, in a discussion of the pleuropericardial syndrome encountered after myocardial infarction, Jaffe[6] wrote: "This type of pericarditis must be separated from the simple, benign, fibrinous pericarditis usually localized, which occurs commonly in acute infarction and may

produce a transitory rub two or three days after the onset, but causes no additional pain or other symptoms or signs and does not influence the clinical course in any way." Of particular interest is the statement made in *Disorders of the Heart and Circulation*, edited by Levy,[7] in regard to the pain of myocardial infarction: "Breathing frequently intensifies the pain. Swallowing, coughing or vomiting may aggravate it, and the patient attempts to avoid them." It would seem that in this description the features of pericardial pain have been attributed to the pain of myocardial infarction.

Description of pericarditic pain after infarction has, however, not been altogether neglected. In his definitive article on coronary occlusion, Herrick,[8] discussing the pathological findings in his patient, wrote: "An acute fibrinous pericardial deposit, which showed no bacteria in smears, was found over the left ventricle. (The pericarditis probably explains the slighter pain complained of a few hours before death.)" Massey,[9] in his discussion of pericarditis epistenocardica, failed to mention the pain associated with this finding. However, in his chapter on pericarditis, he wrote: "Pleuro-pericarditic pain with myocardial ischemia, developing because of an overlying pericarditis, is delayed at least 24 to 48 hours in its appearance." Miller[10] wrote in 1950: "Fresh pain, and as bad as the original agony, may be due to . . . pericardial involvement." A fuller treatment of the subject is to be found in Friedberg's book[11] on diseases of the heart in which is written: "When a pericardial rub discloses the existence of an acute fibrinous pericarditis, there may be no distinct change in the pain; occasionally, however, a recurrence or intensification of pain suggest a relationship to the pericardial lesion, or the precordial pain becomes intensified by deep respiration. Sometimes there are two distinct types of pain, a constant retrosternal pain characteristic of the myocardial infarction, and a pericardial (pleuro-pericardial) sharp pain related to deep respiration."

However, for the most precise and properly emphasized description of the pericarditic pain, we must turn to the book on coronary artery disease by Boas and Boas.[12] Their description follows: "Pericarditis may provoke sharp stabbing precordial pain, often in the region of the apex, aggravated by respiration. Such pain occurring a few days after a coronary artery occlusion is often mistaken for evidence of extension of the arterial thrombus. The nature of the pain, so similar to pleuritic pain should enable the physician to avoid this error."

For the production of pain the pericardium borrows its sensitive neighbor, the pleura. The pericardium itself is apparently insensitive, but by inflammatory involvement of the contiguous pleura it sometimes produces pleuritic pain. The pain of pericarditis is typically respiratory in character and is precipitated or aggravated by breathing, swallowing, coughing, and other movements of the chest. It may be situated in the substernal region, in the epigastrium, in the left hemithorax and left arm, and in the left trapezial region or root of the neck. This is especially well illustrated in the history of the second patient.

The following points about pericardial involvement by infarction are worthy of emphasis and constitute the chief reasons for this presentation:

Pain may be absent or so mild as to escape the notice of both patient and physician. The pain must be specifically sought out, and when its respiratory character is recog-

nized, it will be identified more often and separated more easily from the pain of infarction.

The pain, coming as it does hard on the heels of the first phase of infarction, may be confused with the original pain and may be mistaken for an extension of the original infarct or even for a pulmonary infarct. The pericardial rub is usually absent or missed because of its ephemeral character.

Of greater importance to the clinician is the exquisite diagnostic importance of the pericardial pain. Sometimes the pain of myocardial infarction is atypical, mild, or short-lived; fever, leukocytosis, or a pericardial rub may be absent; the electrocardiographic changes may be obscure or may not appear for several days or even a week. Under such circumstances the appearance of respiratory pain one to several days after an episode of anginal pain is a unique event, which may be considered characteristic of transmural myocardial infarction.

SUMMARY

In a certain number of cases of myocardial infarction, the characteristic crushing pain is closely succeeded by another type of pain, which may be mistakenly attributed to further infarction. That this is not so is attested by its distinctly respiratory nature and by its occasional association with the appearance of pericardial friction, as in the two case histories cited here. It is the contention of the author that pericarditis resulting from myocardial infarct is responsible for this pain. Furthermore, the unique succession of ischemic pain by the pain of pericarditis is pathognomonic of acute transmural myocardial infarction even in the absence of other confirmatory findings.

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Spiramycin in the Treatment of Infections in Children: In Vivo and in Vitro Studies

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Spiramycin[1] is highly effective against gram-positive cocci. The characteristics of this antibiotic were recently reviewed.[2, 3]

In studies on the use of antibiotics in pediatrics,[4–9] a number of observations on 102 spiramycin-treated children were made. They are the subject of the present report.

MATERIALS AND METHODS

One hundred and two children from 12 days to 24 months of age constituted the clinical material. The diagnoses were as follows: purulent pleuritis, 9 children; pneumonia, 18 children; furunculosis, 17 children; septicemia, 10 children; otitis media, 19 children; diarrhea with otitis media and anthritis, 14 children; pharyngitis, 15 children.

One should stress that all these children who qualified for spiramycin treatment were selected from a group of 573 children because of ineffectiveness of previous treatment with other antibiotics. Only 4 infants not treated previously with other chemotherapeutics were given spiramycin at the onset of illness (as the first antibiotic).

Dosage. Spiramycin was administered orally in a dosage of 40 to 60 mg./Kg. for 8 to 10 days and in some cases for 20 days. Supplementary treatment was given when necessary.

White blood cells counts and erythrocyte sedimentation rates were determined serially in all cases. Body weight and temperature were taken daily. Special attention was given to the children's appetite and general feeling and the possibility of side effects of spiramycin.

Criteria of estimating the results of treatment with spiramycin were as follows: improvement in general condition and recession of local lesions; normalization of temperature or a considerable lowering; normalization of white blood cell count and erythrocyte sedimentation rate; negative cultures.

Bacteriological observations were performed strictly as described previously.[10]

Determination of the sensitivity of isolated bacteria to penicillin, streptomycin, chlortetracycline, oxytetracycline, and chloramphenicol was performed by the disc method* according to Gawenda-Dzierzynska and Wasiewicz.[11] Degrees of sensitivity to oleandomycin, oleandomycin-tetracycline, tetracycline, spiramycin, and erythromycin† were determined according to Foulke and Romansky.[12]

* Discs were obtained from Warszawska Wytwornia i Surowic i Szczepionek, Warsaw, Poland.

† Source of standards: oleandomycin and oleandomycin-tetracycline, Pfizer International Subsidiaries, Folkestone, Kent; spiramycin, S.P.E.C.I.A., Paris; erythromycin, Les Laboratoires Roussel, Paris; and tetracycline, Upjohn International Operations, Kalamazoo, Michigan.

RESULTS

In diagnosing staphylococcal septicemia, in addition to several positive blood cultures, a number of symptoms constituting its clinical picture were taken into account (blood circulation, nervous and hematological disturbances). The clinical condition of these children at the moment of admission to the clinic was usually very poor. The results of treatment with spiramycin should be estimated as good. Complete recovery was obtained in 4 cases, very marked improvement in 3 cases. In 1 infant spiramycin did not control the illness, and 2 children died in spite of the intensive treatment.

Table I shows the results of spiramycin treatment.

Of 9 infants with purulent pleuritis, complete recovery was obtained in 5 cases. Previous treatment with penicillin, streptomycin, and chloramphenicol had been unsuccessful. In 2 cases spiramycin produced pronounced improvement, but not complete recovery. The remaining 2 infants, aged 8 and 12 weeks, respectively, died. One must stress that this disease almost always proves fatal in such young infants.

Particularly good results were obtained in the group of 17 children with numerous abscesses of the skin of staphylococcal etiology. These children were admitted to the clinic in poor condition, with symptoms of toxemia, enlarged lymph nodes, and a considerable weight deficiency. Thirteen infants of this group recovered completely; they had been previously treated for long periods with several chemotherapeutic agents. In the remaining 4 cases, the results of treatment should also be considered very satisfactory. These were the children in whom the first symptoms of furunculosis occurred; they had not been previously treated with any antibiotic and were also completely healed after spiramycin therapy. In all these children a fall of temperature was observed in one to four days. The local symptoms also disappeared very quickly, which was especially noted in these 4 cases.

Results of treatment were also extremely good in the 15 cases of pharyngitis. The local inflammatory changes disappeared quickly (in one to four days) and the swollen lymph nodes of the neck returned to normal. White blood cell count and erythrocyte sedimentation rate became normal during administration of the antibiotic. General condition and feeling improved as the appetite of the infants increased rapidly and distinctly.

Eighteen children with pneumonia constituted the next spiramycin-treated group. In 10 cases the results should be considered very good. The temperature was reduced within 36 to 72 hours, and the recession of inflammatory changes in the lungs was observed in the first stage of the treatment. Dyspnea disappeared quickly and the blood circulation improved. In the next 2 cases it was not possible to stop the progress of illness, and an exudative pleuritis followed. These infants, aged 4 and 5 months, respectively, had previously been treated with penicillin, streptomycin, and chloramphenicol without result. In the remaining 6 cases of pneumonia, improvement was considerable, although complete recovery was not achieved.

The results of spiramycin treatment should also be considered good in 19 cases of purulent otitis media of mixed streptococcal-staphylococcal etiology. The disease was chronic and lasted, in some cases, from 18 to 37 days with several recurrences and

TABLE I

Results of Treatment of 102 Children with Spiramycin

Diagnosis	No. of children	Previous treatment*	WBC/ESR			Weight			Stools			Temperature			Result		
			Increase	No change	Normalization	Decrease	No change	Increase	Change for worse	No change	Improvement	Increase	No change	Decrease	Very good	Satisfactory	Negative
Septicemia	10	P, S, N, C	2/0	1/2	7/8	2	3	5	—	9	1	2	1	7	4	3	3
Pneumonia	18	P, S, C	1/2	5/6	12/10	6	2	10	—	17	1	2	2	14	10	6	2
Pleuritis	9	P, S, C	2/1	3/3	4/5	4	3	2	—	9	—	1	3	5	5	2	2
Furunculosis	17	P, S, C†	—	3/5	14/12	—	7	10	—	17	—	—	—	17	17	—	—
Pharyngitis	15	P, S, SU	—	4/5	11/10	—	5	10	—	15	—	—	1	14	15	—	—
Otitis media	19	P, S, C, SU	—	9/12	10/7	4	4	11	—	19	—	—	12	7	10	7	2
Toxic diarrhea with otitis	14	CL, SG, P, S, C	2/5	9/4	3/5	6	5	3	4	6	4	2	8	4	4	—	10
Total	102		7/8	34/37	61/57	22	29	51	4	92	6	7	27	68	65	18	19

WBC = White blood cell count, ESR = erythrocyte sedimentation rate.

* P = penicillin, S = Streptomycin, N = novobiocin, C = chloramphenicol, SU = sulfathiazole, CL = chlortetracycline, SG = sulfaguandine.

† Four children in this group had not received any antibiotic treatment previously.

changes for the worse. All these children had previously been treated with other antibiotics without positive results. Complete recovery was reached in 10 cases and pronounced improvement in 7 cases; in only 2 cases did treatment fail. The illness in these 2 infants, aged 5 and 6 months, respectively, had lasted six and nine weeks, respectively.

Fourteen children with toxic diarrhea complicated by purulent otitis media and anthritis constituted the last group. All these children had previously been treated or had been in pediatric wards of the district hospitals. The illness lasted from 20 to 35 days, or became worse. In this group, complete recovery, i.e., disappearance of the purulent exudate from the ears and of the diarrhea, was obtained in only 4 cases. In the 10 remaining cases, on the other hand, only pronounced reduction of the pus from the ears was observed, while the diarrhea persisted. In 4 cases anthrotomy was performed. Spiramycin treatment in the postoperative period gave very good results, as shown by lowering of temperature, rapid healing of wounds, increase of appetite, increase in weight, etc. (as compared with untreated children).

Great tolerance to spiramycin was observed. Sporadic vomiting was noted in 5 cases and transitory rash in 3 cases.

A total of 297 coagulase-positive strains were isolated from the treated children (194 strains came from the patients in different periods of illness and 103 from carriers). All the strains were tested for sensitivity to nine antibiotics and one combination of antibiotics. The results of tests in vitro suggested a division of these drugs into three groups, according to the number of resistant strains isolated from patients: group 1: oleandomycin-tetracycline, 10 resistant strains; spiramycin, 12 resistant strains; oleandomycin, 13 resistant strains; erythromycin, 16 resistant strains; chloramphenicol, 23 resistant strains; group 2: tetracycline, 52 resistant strains; oxytetracycline, 55 resistant strains; chlortetracycline, 57 resistant strains; group 3: streptomycin, 95 resistant strains; penicillin, 154 resistant strains.

The degree of sensitivity of staphylococci isolated from the carriers closely resembled this pattern. The details are given in table II.

The activity of the erythromycin group of antibiotics and chloramphenicol was the greatest. No pronounced changes of sensitivity were observed in strains isolated from patients before and during treatment. The percentage of antibiotic-resistant strains before treatment was 33.8 and after treatment, 35.2. The change was thus negligible. This was not the case with antibiotic-resistant strains isolated from carriers. Before starting therapy, the percentage of resistant strains was 24.8, while when the carriers left the clinic it was 28.1. Also, an interesting phenomenon was observed in the erythromycin group of antibiotics. None of these children was a carrier of erythromycin-resistant or spiramycin-resistant strains on arrival at the clinic, but 10 such strains were isolated from their throats at the time of leaving.

One hundred and forty-three strains of staphylococci isolated from pathological material and 51 strains of these microorganisms isolated from the throats of carriers were studied for the presence of several toxic and biochemical properties associated with pathogenicity (table III). No significant differences between staphylococci from pathological processes and from the throat were found. If strains were coagulase positive, they excreted several toxins and possessed various biochemical properties,

TABLE II

Action of Penicillin, Streptomycin, Chloramphenicol, Chlortetracycline, Oxytetracycline, Tetracycline, Oleandomycin, Oleandomycin-Tetracycline, Erythromycin, and Spiramycin on Staphylococci Isolated from Pathological Material and Carriers

Source of strains	No. of strains examined	Number of strains																			
		Penicillin		Strepto-mycin		Chloram-phenicol		Chlor-tetra-cycline		Oxytetra-cycline		Tetra-cycline		Oleando-mycin		Oleando-mycin + tetra-cycline		Erythro-mycin		Spira-mycin	
		S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R
From pathological material before treatment	104	21	83	49	55	90	14	73	31	75	29	76	28	98	6	99	5	97	7	99	5
From pathological material during treatment	90	19	71	46	44	81	9	64	26	64	26	66	24	83	7	85	5	81	9	93	7
Total from pathological material	194	40	154	95	99	171	23	137	57	139	55	142	52	181	13	184	10	178	16	182	12
From carriers at admission to clinic	31	20	11	23	8	27	4	25	6	26	5	26	5	30	1	31	—	31	—	31	—
From carriers leaving clinic	72	31	41	36	36	63	9	54	18	54	18	56	16	66	6	68	4	67	5	67	5
Total from carriers	103	51	52	59	44	90	13	79	24	80	23	82	21	96	7	99	4	98	5	98	5
Total from pathological material and carriers	297	91	206	154	143	261	36	216	81	219	78	224	73	277	20	283	14	276	21	280	17

S = sensitive strain, R = resistant strain.

TABLE III

Occurrence of Various Toxic and Biochemical Properties in Staphylococci Isolated from Pathological Material and Carriers

	Strains isolated from pathological material (143)	Strains isolated from carriers (51)
Free coagulase	143	51
Bound coagulase	143	50
α-hemolysin	137	47
β-hemolysin	62	4
δ-hemolysin	140	51
Leukocidin	142	46
Staphylokinase	130	46
Urease	132	35
Lipase	136	44
Gelatinase	144	51
Phosphatase	142	49
Aureus pigment	139	47
Anaerobic fermentation of mannitol	143	51
Anaerobic fermentation of glucose	143	51
Growth in normal human serum	143	48

considered by several authors as criteria of potential pathogenicity. Also the coagulase titer of the cell-free culture supernatant, as shown in table IV, did not demonstrate the existence of any correlation between source of strain and amount of free coagulase excreted in vitro. Similar observations were noted in large numbers of staphylococci.[13, 14]

DISCUSSION

The best clinical results were obtained with spiramycin in infections of staphylococcal etiology, which is in accordance with the results of tests in vitro. As might be expected, spiramycin treatment is not effective for diarrhea, in which gram-negative bacilli are dominant. The high tolerance of spiramycin should be stressed. Side effects, observed in 8 of 102 cases, were very mild, and it was not necessary to stop treatment. As may be observed from the results of sensitivity tests in vitro,

TABLE IV

Free Coagulase Titer and Source of Strain

Source of strain	Number of strains studied	Free coagulase titer			
		0*	1:10–1:1280	1:640–1:1280	1:2560 or more
Clinical material	143	43	60	33	7
Carriers	51	16	14	14	7

* Clotting of plasma with living cultures only.

spiramycin may be considered one of the most effective antistaphylococcal antibiotics. Together with other antibiotics of the erythromycin group and chloramphenicol, it is one of most effective antibiotics that may be used against these bacteria at present. Bacteriological observations concerning distribution of various toxins and biochemical properties of staphylococci in relation to their source showed no correlation between these phenomena. Pathogenicity of staphylococci is as yet unknown, and laboratory tests for excretion of these factors play an auxiliary role. Moreover, in our opinion, at this time there is no single test for the pathogenicity of staphylococci; eventually this may be shown by determining several toxic and biochemical properties of staphylococci. As shown in other studies, these include: α- and δ-hemolysins, free and bound coagulases, leukocidin, ability to grow in normal human serum (determined quantitatively), anaerobic fermentation of mannitol and phosphatase.[13–16]

SUMMARY

One hundred and two children, aged 12 days to 24 months, were treated with spiramycin. The children had the following illnesses: purulent pleuritis, 9; pneumonia, 18; furunculosis, 17; septicemia, 10; otitis media, 13; pharyngitis, 15; toxic diarrhea complicated by purulent otitis media and anthritis, 14. The drug was given orally in a dosage of 40 to 60 mg./Kg. daily in four divided doses. The best results were obtained in pharyngitis and furunculosis, as all the children recovered very quickly. Good results were also obtained in all other infections except that of complicated toxic diarrhea. In this group, only 4 of 14 children responded to spiramycin treatment. Of the total of 102 children, very good results were obtained in 65 cases, satisfactory in 18 children, and no improvement in 19 patients, all of whom had diarrhea. Staphylococci were isolated from the pathological material, as well as from the throats of carriers, before, during, and after treatment. A total of 297 strains were tested for sensitivity to penicillin, streptomycin, chlortetracycline, oxytetracycline, chloramphenicol, tetracycline, oleandomycin, oleandomycin-tetracycline, spiramycin, and erythromycin. It was found that these strains were most susceptible to the action of antibiotics from the erythromycin group (spiramycin, oleandomycin, and erythromycin), oleandomycin-tetracycline, and chloramphenicol. The number of resistant strains harbored by carriers was greater at the time of leaving the clinic. No serious symptoms of intolerance of spiramycin were observed. One hundred and ninety-three strains of staphylococci were studied for ability to form various toxins and for possession of several biochemical properties (α-, β-, and δ-hemolysins, free and bound coagulases, staphylokinase, leukocidin, urease, lipase, gelatinase, phosphatase, *aureus* pigment, anaerobic fermentation of mannitol and glucose, ability to grow in normal human serum). Eventual correlation between the source of strains and free coagulase titer in staphylococcal culture in vitro was investigated.

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Therapeutic Action of Tetracycline-Oleandomycin Combination in Severe Infections of the Respiratory Tract

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CHEST CLINIC

ROSARIO, ARGENTINA

Tetracycline-oleandomycin combination* has been studied by several investigators, who have pointed out, among various properties, its broad spectrum, the synergism of its components, its efficacy against strains resistant to other antibiotics, and particularly its effectiveness against pathogenic *Staphylococcus aureus*.[1–10]

Because of the increased frequency of staphylococcic infections, we decided to carry out this therapeutic trial with the tetracycline-oleandomycin combination in a series of patients at our clinic, at which are seen only patients with respiratory tract disease.

MATERIAL AND METHODS

We prescribed the antibiotic combination for 41 patients, who were divided into six groups. Diagnoses and ages of these patients are shown in table I.

In severe adult cases tetracycline-oleandomycin was administered in an initial dosage of 1.5 to 2.0 Gm. orally, given until normalization of temperature; then 1.0 Gm. was given daily. In the less severe cases, a dosage of 1.0 Gm. daily was used throughout treatment. In children, daily oral dosage was determined according to body weight. Dosage varied, depending on the severity of the disease, from 20 to 60 mg./Kg./day. Duration of treatment varied also; in pleural empyema treatment was prolonged until normalization of clinical and roentgenological manifestations and laboratory tests for infection, although in most cases, treatment was continued with open drainage. In the group of patients with abscesses, administration of the antibiotic combination was prolonged to avoid relapses. In asthmatic patients and patients with cor pulmonale and cystic fibrosis of the pancreas, the antibiotic therapy was prescribed in acute episodes. In patients operated on for bronchiectasis with infection, the drug was prescribed during the immediate pre- and postoperative period.

Depending on the clinical picture, the following additional treatment was given: early surgical drainage in pleural empyema, due to minimum pleurotomy; bronchoaspiration in two pulmonary abscesses; resection for mechanical disorders of vesicles in obstructive emphysema with infection, after the infection was cured; in several cases of pleural and bronchopulmonary infection, administration of prednisolone or prednisone in dosages of 15 to 20 mg. daily in adults and 5 to 10 mg. daily in children; when administration of the antibiotic was prolonged, addition of vitamin B complex.

* The trade name of Chas. Pfizer & Co., Inc., for a combination of tetracycline and oleandomycin is Signemycin.

Bacteriological studies were carried out in all the cases. In pleural empyema, pure cultures of the causal bacteria were used for sensitivity tests. In other cases, in order to expedite testing, pools of isolated bacteria from sputum were used. The tube dilution method and the disc diffusion method were used for tests of sensitivity.

As was anticipated, when the study material contained only one species (empyema), the antibiotic activity was more evident on macroscopic observation of dilution tubes than in a pool of bacteria (sputum); likewise, the dilution method was superior to the diffusion method. No dilution of drugs kept for more than 15 days was used.

RESULTS

In all patients with acute pleural empyema, response to the antibiotic treatment was favorable and rapid. The temperature quickly dropped to a normal level after 24 to 36 hours in almost all cases, remaining at subfebrile level in a few patients for several days.

Improvement of the general condition and reabsorption of the uni- or bilateral parenchymatous component, when it was present, were also observed.

In all these patients drainage due to minimum pleurotomy with aspiration under water was prescribed early except in an 8-year-old child, who was cured rapidly with the antibiotic alone.

The following case report is typical of this group.

CASE 1. An 8-year-old boy was admitted with a diagnosis of acute pleural empyema. The condition had started 15 days before admission on Dec. 8, 1958. The patient had had a continuous fever, which was treated with oxytetracycline and chloramphenicol. The temperature declined, but did not reach normal levels; it rose again and there was dyspnea and deterioration of the general condition. At admission, clinical examination revealed definite signs of pleural effusion. Roentgenographic examination at this

TABLE I

Diagnoses and Ages of 41 Patients Treated with Tetracycline-Oleandomycin

Group	Diagnosis	No. of patients	Age
1	Acute pleural empyema	5	2–12 mo.
		9	5–11 yr.
2	Acute abscess of lung	3	30–47 yr.
	Obstructive emphysema with infection	1	7 mo.
	Acute sinusitis with pneumonitis	1	10 yr.
3	Bronchopulmonary infection with cystic fibrosis of the pancreas	3	5– 8 mo.
4	Recurring acute bronchial infection in asthmatic patients with chronic bronchitis	12	5–25 yr.
5	Chronic bronchitis with pulmonary fibrosis and emphysema complicated by chronic cor pulmonale	5	50–65 yr.
6	Bronchiectasis with infection	2	19–20 yr.

time revealed opacity of the right hemithorax with a pleural aspect, blurring of the costodiaphragmatic sinus, and peripheral pulmonary density. Laboratory findings were as follows: anemia of 3,800,000 red blood cells with 70 per cent hemoglobin; leukocytosis of 15,600 with frank neutrophilia of 80 per cent; accelerated erythrosedimentation, 37 to 70 mm.; Katz's index, 36 mm. The urine had a density of 1019, with albumin traces; there was frank urobilinuria, with limited hyaline casts and slight pyuria. By pleural puncture, 200 ml. of purulent liquid was removed and gave the following findings: Rivalta's reaction, +++; 79 per cent, polymorphonuclear neutrophils; 15 per cent, lymphocytes; 6 per cent, other cells. Pathogenic *Staph. aureus* was isolated.

The patient was treated with penicillin, streptomycin, erythromycin, prednisone, blood transfusions, vitamin C, administered intravenously, and multiple vitamins, administered orally. In spite of this therapy, the toxic infectious condition persisted. After seven days, these antibiotics were withdrawn and tetracycline-oleandomycin was administered, 1 Gm. daily, divided into doses of 250 mg. every six hours, given orally. The prednisone and vitamins were continued. After 26 hours, a clinical improvement was observed and the temperature level had decreased to 37 to 37.6 C. Three weeks later, roentgenogram of the chest anteriorly and laterally revealed a hydroaerial image of a pleural cavity. Seventeen days later, this image was observed to be in regression. The antibiotic dosage was reduced to 750 mg. daily for one month. Final roentgenograms taken March 6, 1959, showed healing of the pleuropulmonary lesions and a complete functional recovery. Tolerance to the antibiotic was good throughout the entire treatment period, a duration of two months and one week.

Three acute abscesses of the lung, localized in the right superior lobe, healed completely with no sequelae. In 2 cases, bronchoaspiration was associated with the antibiotic medication. The following case is typical.

Case 2. J.E.B., a 41-year-old man, had a diagnosis of acute abscess of the lung. The condition started 12 days before admission, on Dec. 28, 1958. The patient was sent to the hospital because of fever, productive cough, and rusty sputum. Roentgenograms taken on admission revealed opacity of the right vertex with a cavitary image with liquid level. Hemogram demonstrated leukocytosis of 10,400, with neutrophilia of 83 per cent and normal values for hematids and hemoglobin. The sputum contained no Koch bacilli, but did contain pneumococci, streptococci, and *Neisseria catarrhalis*. Urine density was 1028; albumin, 0.60 Gm. /100 ml.; and there were some granulous cylinders. Urea in the blood was 0.30 Gm. /100 ml.

Tetracycline-oleandomycin was administered in a dosage of 2.0 Gm. orally for the first three days and thereafter 1.5 Gm. daily and 15 mg. daily of prednisolone. Improvement was rapid. Two weeks later, roentgenogram of the pulmonary vertex showed persistence of the cavitary image without liquid level. After 40 days of treatment, another roentgenogram showed complete healing of lesions.

A child aged 7 months, with obstructive emphysema with infection, localized in the left lung, was treated similarly. The infection was cured. Resection of the residual cavity was advised, but not carried out. In a patient with acute sinusitis complicated by aspiration pneumonitis, treatment was also successful.

In 12 patients with chronic asthma and 5 with chronic cor pulmonale, periodic administration of the antibiotic combination in acute bronchial episodes yielded excellent results, which were comparatively greater than those obtained with other antibiotics of both small and broad spectrum.

In 3 infants with cystic fibrosis of the pancreas, tetracycline-oleandomycin was effective and allowed recovery of the patients from the severe and extended acute bronchopulmonary complications consequent to bronchiolar obstruction, which, as is well known, are the cause of death, in infants, in 50 per cent of cases of interstitial bronchopneumonia and bronchiectasis, with frequent formation of abscesses.[11] In these cases, the antibiotic combination was useful in prolonging life.

A typical case history follows.

CASE 3. L.M.S., a female infant, was 10 months old at the time of the first admission. The diagnosis was cystic fibrosis of the pancreas, chronic diffuse pneumonitis, and bronchiectasis. The infant's father was asthmatic, her sister suffered from allergies, and her mother had had relapsing bronchitis until the age of 12 years. The patient's condition had begun when she was 1 month old, with cough, expectoration, and steatorrhea. She was frequently in a febrile state and had had influenza. On admission, on Aug. 22, 1958, clinical examination showed delayed growth, undernourishment, and a tympanic abdomen; auscultation of the thorax demonstrated subcrepitant stertors, rhonchi, and whistlings in both lungs. Percussion revealed normal sonority. Roentgenogram of the chest revealed nodular and linear images in both pulmonary areas, which demonstrated an alteration in the normal structure. There was leukocytosis of 19,000; leukocytes and neutrophilia of 80 per cent; normal values for hematids and hemoglobin. There was a negative reaction to tuberculin. The sweat test, with determination of sodium and potassium levels, was frankly positive. There was a febrile syndrome (38.2 C.); steatorrhea was proved.

Tetracycline-oleandomycin was administered in a daily dosage of 50 mg./Kg., given orally in divided doses. Vitamin B complex and nystatin were also given as complementary therapy. After three days, the temperature dropped and remained subfebrile for seven days, finally becoming normalized; improvement in the general state and slight increase of weight were observed. Regression of local pulmonary symptoms was demonstrated at auscultation. Roentgenogram showed total regression of the nodular elements of the pulmonary parenchyma, with persistence of some linear elements of tramitis. After 10 days, the acute pulmonary lesions became normalized. After this acute pulmonary episode, the patient had three similar episodes, each time responding rapidly to tetracycline-oleandomycin, which was always well tolerated. In January the patient was readmitted with a febrile syndrome and total atelectasis of the right lung, with diminution of the vesicular murmur and subcrepitant stertors; there was frank leukocytosis with neutrophilia. The same dosage of tetracycline-oleandomycin was administered, with mucolytic medication and prednisolone. Later, better ventilation of the right lung was observed; however, typical images of bronchiectasis remained in this pulmonary area. The infant's condition became worse, and she died on Feb. 17, 1959 (a very hot day), with a clinical picture of dehydration and circulatory collapse despite the therapeutic measures. Post-mortem examination revealed cystic fibrosis of the pancreas, bronchiectasis in areas of alveolitis, chronic pneumonitis, and a normal liver.

In patients with bronchiectasis with infection who were operated on, the antibiotic combination and prednisolone were administered during the immediate pre- and postoperative periods to permit surgical intervention without difficulty and to prepare for convalescence free of complications.

Summarizing, of a series of 41 cases, we obtained satisfactory therapeutic results in all but 2 patients with cor pulmonale and severe infections, in whom the antibiotic combination cleared all bacteria of mixed flora found in the sputum; later there appeared moniliasis due to *Candida albicans*, which was controlled with adequate treatment. In a few cases we observed softness of the stools or slight diarrhea, which did not make it necessary to stop the antibiotic treatment.

In the remaining patients, tetracycline-oleandomycin was well tolerated, even on prolonged administration.

In some cases, bacteriological study by the tube dilution method permitted us to observe in vitro significant findings on the sensitivity of tetracycline-oleandomycin, which confirmed the synergism of its components, already proved by other investigators.[1] Results obtained are shown in table II.

Our findings show that, in some cases, the antibiotic combination can be more active than its two components alone or their sum and that the combination can be effective despite resistance to one or both components simultaneously.

TABLE II

Results of Sensitivity Tests of Microorganisms Isolated from Samples Obtained in Some Patients (Dilution Method)

Microorganism and diagnosis	Minimum inhibitory concentration, μg./ml.		
	Oleandomycin-tetracycline	Tetracycline	Oleandomycin
Coagulase-positive *Staph. aureus*; isolated in pure culture of acute pleural empyema in a child aged 5 mo.	0.625	1.25	5
Coagulase-positive *Staph. aureus*; isolated in pure culture of acute pleural empyema in a child aged 3 mo.	0.625	0.625	2.5
Coagulase-positive *Staph. aureus*; isolated in pure culture of acute pleural empyema in a child aged 5 yr.	2.5	5	0
Pool of microorganisms (sputum) with predominance of pneumococcus; acute abscess of lung in adult patient (case 2)	2.5	0	0
Pool of microorganisms (sputum) with predominance of pneumococcus; acute abscess of lung in adult patient	2.5	5	0
Pool of microorganisms (sputum) with predominance of *Staph. aureus* and pneumococcus; acute abscess of lung in adult patient	2.5	5	5
Pool of microorganisms (sputum) with predominance of pneumococcus; vesicle of infected emphysema in child aged 7 mo.	2.5	2.5	0

COMMENT

In laboratory investigations to isolate the bacteria of pleural empyema, we observed a variety of bacteria causing infection. In 1956, *Staph. aureus* was the exclusive etiological agent in 46 per cent of cases; in the remaining cases, the organism was pneumococcus alone or with *Streptococcus*. Our studies in 1959 led us to believe that 100 per cent of acute pleural empyemas in children are caused by *Staph. aureus*; we have not observed any additional organisms. This emphasizes the importance of infections caused by staphylococci and points up the usefulness of antibiotics that are really effective against staphylococci. Tetracycline-oleandomycin proved to be effective even in cases where the microorganisms were resistant to other commonly used antibiotics, as noted previously.

Our findings with regard to sensitivity of the antibiotic combination and of each of its components lead us to believe, with other investigators, that its activity results not from the addition of its components, but from potentiation due to synergism of tetracycline with oleandomycin. This explains the excellent results obtained by us in these cases, even where there was partial or simultaneous resistance to these antibiotics.

The satisfactory results obtained with tetracycline-oleandomycin and its particular effectiveness in staphylococcic infections, which we have seen with increased frequency, lead us to consider it the antibiotic of choice in severe infections of the respiratory tract. Prednisolone and prednisone, added to the antibiotic therapy, seem to be useful for these patients, in whom the additional drugs aided reabsorption of pleural and bronchopulmonary exudations.

SUMMARY AND CONCLUSIONS

Satisfactory results obtained with tetracycline-oleandomycin in a series of 41 patients, most of whom had severe infections of the respiratory tract, lead us to consider this antibiotic the therapy of choice in this type of infection.

We have demonstrated the particular effectiveness of this antibiotic combination against staphylococcic infections, whose incidence has increased recently.

In some cases in this series, tests of sensitivity by the dilution method confirmed the existence of synergism between both components, even when there was partial or simultaneous resistance. This would explain the excellent therapeutic results obtained in patients with acute pleural empyema and acute abscess of the lung.

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The Use of the Appetite Suppressant Benzphetamine in General Office Practice

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The commonest form of malnutrition in the United States is obesity. It has been estimated that 15,000,000 people are 10 per cent overweight and that 5,000,000 of these are 20 per cent overweight. At least several million of these people have tried, or are trying, to lose their excess poundage.

The general practitioner is continually called on to assist these people with encouragement and advice as to diet and exercise. He is also the one who must decide whether so-called anorexiant drugs may be helpful and which of the many available drugs to prescribe. Treating, as he does, a wide variety of acute and chronic diseases, he must be satisfied that whatever drug he uses will be efficacious promptly and over prolonged periods. It must not interfere in the management of other diseases, for example, diabetes mellitus or hypothyroidism. Perhaps most important, it should have appetite-suppressing qualities without side effects that might aggravate coexisting illnesses such as hypertensive cardiovascular disease or coronary insufficiency.

It is the purpose of this paper to report our experience with a new drug that appears to meet these requirements, benzphetamine hydrochloride (Didrex).||

MATERIALS AND METHODS

Altogether we studied 60 obese patients who fell into the following diagnostic categories: chronic, refractory obesity, 22; hypertensive cardiovascular disease, 14; diabetes mellitus, 12; hypothyroidism, 8; arteriosclerotic heart disease, in failure, 2; coronary arterial disease, 2. The patients ranged in age from 13 to 71 years; 21 were men.

Treatment for obesity involved advice on diet in an effort to limit daily caloric intake to less than 1200. Benzphetamine was started in all instances with one or one half of a 50 mg. tablet given in mid-morning. Patients were seen frequently and dosage was increased or decreased to obtain optimal appetite suppression with minimal side effects. We tried to "tailor" the dosage to each patient's needs.

Pilot urine and peripheral blood studies were done; kidney and liver function studies were performed at least once on each patient. Electrocardiographs and chest

Part of this work was done with the cooperation of members and officers of the Restaurant, Dining Room and Luncheonette Employees Union Local 1115.

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|| The trade name of The Upjohn Co. for benzphetamine hydrochloride is Didrex.

roentgenograms were also taken. In addition, it was necessary in more than half our series to manage actively a secondary disease such as diabetes mellitus or cardiac failure.

RESULTS

It can be said at the outset that results were very gratifying. In table I are shown the number of patients who, during the course of several days or weeks, arrived at dosage regimens that seemed optimal for their individual requirements. These varied from 6 who did well on only one half tablet (25 mg.) of benzphetamine twice daily to 1 who felt his best response was achieved on a dosage of 100 mg. before each meal.

In treatment periods varying from 6 to 26 weeks (average 19.4), all patients but 2 lost weight. In a total of 1163 patient weeks, 813.75 lb. were lost, or 13.56 lb./patient. Expressed another way, average loss per patient per week was 0.70 lb.

The performance index for a weight reduction program may be determined by dividing the actual pounds lost in a given period by the pounds of excess weight (over the "ideal" for a given height, age, sex, and body frame) times 100. If a patient begins treatment weighing 50 lb. over his ideal weight and loses 25 lb., his performance index would be 50 per cent. The over-all performance index in this study was 34.6 per cent.

A particularly difficult group of patients was that comprising the 22 with chronic, refractory obesity. All had tried unsuccessfully to lose weight one or more times in the past. All types of medication had been used with varying results in terms of appetite suppression and side effects. It was gratifying to note that only 4 of these patients failed to lose weight during this study. The following case summary was typical.

CASE 1. J. B., a 44-year-old chronically obese man, had taken the gamut of drugs through the years. He was extremely sensitive to central nervous system side effects of anorexiants but finally achieved satis-

TABLE I
"Tailored" Dosage Regimens

No. of patients	No. of tablets				Times/day				Total mg.
	½	1	1½	2	1	2	3	4	
6	X					X			50
18	X						X		75
4	X							X	100
8		X				X			100
14		X					X		150
4			X			X			150
2			X				X		225
3				X		X			200
1				X			X		300

Starting with one or one half of a 50 mg. tablet in mid-morning, the dosage of drug was changed frequently until these regimens were arrived at.

factory appetite suppression by taking 25 mg. of benzphetamine three times daily. He lost weight steadily though slowly and improved psychologically. He gradually became more cooperative and cheerful and for the first time agreed to undergo psychotherapy. Weight change was a loss of 15.5 lb. in 20 weeks.

It is axiomatic that patients with hypertensive cardiovascular disease should be at or even slightly below "ideal" weight. It is also most important that no medication be given that will further elevate blood pressure. Of the 14 patients studied, all lost weight. Elevation in blood pressure, even after as much as 24 weeks' continuous administration of benzphetamine, was not observed. In some patients, on the contrary, systolic pressures tended to fall as weight reduction occurred.

CASE 2. B. L. was a 58-year-old woman with hypertensive heart disease of six years' duration. She had tried various drugs for reducing purposes, all to no avail. There was either lack of appetite suppression or untoward reactions. A benzphetamine regimen was finally "tailored" to 25 mg. three times daily and she reduced from 162.5 to 143 lb. Her "ideal weight" was 145 pounds.

Four of the 12 patients with diabetes mellitus were taking insulin; the remaining 8 were taking from 1 to 3 tolbutamide tablets daily (0.5 to 1.5 Gm.). Benzphetamine in no way interfered with, or altered requirements for, these medications. All patients lost weight during the study. The following case was typical.

CASE 3. D. N., a 39-year-old diabetic man, was also chronically obese. Originally on insulin, he had been switched to tolbutamide one year previously. The patient's diabetes mellitus was not well controlled with one 500 mg. tablet twice daily until a "tailored" dosage regimen of 50 mg. of benzphetamine was worked out. The diabetes then became well controlled and the patient did well, dropping from 190 to 167 lb. (23 lb. loss) in 20 weeks.

The hypothyroid group was, again, highly refractory to weight reduction. By manipulating the dosage of benzphetamine frequently to obtain optimal effect, however, good weight loss was obtained in 7 of 8 patients.

CASE 4. H. K., a 33-year-old woman, complained of chronic fatigue, listlessness, constipation, and weight gain. Cholesterol (normal 150 to 250 mg./100 ml.) was 295; serum protein–bound iodine, 2.4 μg.; I^{131} uptake, 14 per cent; basal metabolic rate, −18. The patient felt better when given thyroid extract but did not lose weight. When given benzphetamine, 25 mg. four times daily, weight reduction began and she lost 18 lb. in 20 weeks.

The patients with arteriosclerotic heart disease with failure (2) and with coronary insufficiency (2) did very well in that all of them lost weight. Serial electrocardiographic tracings were taken and either remained unchanged or showed improvement with the passage of time.

There were no significant side effects requiring cessation of treatment except for a skin rash in 1 patient, which may have been drug related. Slight central nervous system stimulation was often noted during the first week but only 1 patient complained of palpitations, another of insomnia. Reduction of dosage solved these problems. Similarly, drug-induced changes in the urinalyses or peripheral blood pictures were not noted, nor were renal or hepatic function tests adversely affected.

DISCUSSION

Benzphetamine hydrochloride is an amphetamine congener that has been the subject of several controlled clinical trials.

Simkin and Wallace,[1] using the double-blind approach, clearly showed anorexigenic activity by comparison with placebo tablets. They reported good weight loss using 75 or 150 mg./day plus a 1000 calorie diet. Side effects in drug and placebo groups were about the same.

Their report was confirmed in controlled trials by Poindexter,[2] Schapiro and Bográn,[3] and Stough.[4] The last writer pointed out that he was aware almost immediately which coded preparation was the active drug because of central nervous system stimulation at the dosage used (150 mg. daily). Oster and Medlar[5] also noted this in men known not to have taken amphetamine drugs in the recent past. These authors carefully observed symptoms and weight changes associated with a regimen of only 25 mg. three times daily. Weight loss was just as good with 75 as with 150 mg. daily, and troublesome side effects were much less. Stough took the next step in this titration and found that single doses of 50 or even 25 mg. given during the morning produced virtually no effect but the desired one, appetite suppression.

It was this background of experience that suggested the dosage "tailoring" we used in this study. Since these data suggested a "split" between desirable and undesirable effects, we hoped to take advantage of this. Stough's findings, together with the experimental design involving private patients, made the use of placebo controls undesirable. Further, Rhoades[6] had presented data on private obese patients given 50 mg. of benzphetamine once, twice, or three times daily. Weight loss was obtained with all three regimens. His encouraging results, plus the fact that he was dealing with office patients from a general medical practice, led us to explore the idea of dosage alteration or "tailoring" in the same type of practice.

Our data support the concept of a "split" between central nervous system stimulation or excitation and appetite suppression due to benzphetamine. It has recently been stated that the likelihood of finding such a compound among amphetamine congeners seemed remote, since none of the presently available ones appeared to induce appetite suppression without stimulation.[7] The facts that 58 of our patients had no complaints relative to stimulation and that 58 of the 60 enjoyed weight loss for periods as long as 24 weeks suggest that benzphetamine may have separable effects, at least when it is used on a flexible, "tailored" regimen.

Results in patients with hypertensive cardiovascular disease, coronary insufficiency, and heart failure were most encouraging. A tendency was noted for elevated systolic blood pressures to fall to lower levels, as has been reported by others.[2, 4, 6, 8, 9] It was felt this would probably have occurred incidental to any successful weight-reduction program. The important aspect of this part of the study was that pressure was not elevated.

Findings in the group of obese diabetic patients were of interest because they showed in diabetic persons what Oster and Medlar[5] had reported in fasting normal volunteers: benzphetamine had no apparent effect on glucose metabolism. The drug did not interfere with the management of diabetic patients with insulin or with oral euglycemic agents, in this case tolbutamide.

Finally, the obese hypothyroid patients responded well. There seems to be a myth that obesity is quite often associated with hypothyroidism. This is not so. As a

matter of fact, it is not at all unusual to observe thin or underweight hypothyroid patients. All of our hypothyroid patients in this study were obese and lost weight on the addition of benzphetamine to their routine thyroid medication. They had failed to do so with thyroid extract alone.

SUMMARY

A new appetite suppressant, benzphetamine hydrochloride, has been studied under conditions of general office practice in a total of 60 patients. Twenty-two were patients with chronic, refractory obesity problems and the remainder were overweight patients having hypertensive cardiovascular disease (14), diabetes mellitus (12), hypothyroidism (8), arteriosclerotic heart disease with congestive failure (2), or coronary insufficiency (2).

Appetite suppression was obtained by starting drug administration with a single mid-morning dose of 50 mg. This dosage was then frequently increased or decreased in an effort to "tailor" it to the optimal regimen required by each patient. During study periods ranging from 6 to 26 weeks, 58 patients lost weight, at an average rate of 0.70 lb./patient/week. Total weight lost in the group was 813.75 lb., or 13.56 lb./patient. Performance index averaged 34.6 per cent.

Tolerance to the drug was excellent using the flexible dosage regimen described. Slight central nervous system stimulation was often noted during the first week but only 1 patient complained of insomnia, another of palpitations. These symptoms were readily controlled by altering dosage. One patient developed a mild rash, possibly drug induced. There was no interference by benzphetamine with the management of concomitant diseases such as hypertension, diabetes mellitus, hypothyroidism, congestive heart failure, or coronary insufficiency.

Altogether, the stimulation was so minor and the appetite suppression so effective and sustained that they appeared to be separate effects. Benzphetamine can be recommended as a safe and effective agent for use in the office management of obesity.

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NEW MICROSCOPE FOR RHEUMATISM RESEARCH. An electronic microscope capable of magnifying 150,000 times is being used in a new clinic for research in rheumatism, at St. Thomas' Hospital Medical School, London. The microscope will magnify the diameter of a cell measuring only one-thousandth of an inch to 15 inches, thus allowing the study of the detailed structure of the cells of cartilage. So far, cartilage has been studied with ordinary compound microscopes that magnify up to 1000 times.

ANTISPASMODIC. A combination of propantheline bromide and phenobarbital (Probital, Searle) is said to be useful for the milder symptoms of gastrointestinal spasm when sedative effects are also required. It is indicated for functional gastrointestinal disorders, pylorospasm, gastritis, biliary dyskinesia, colonic spasm, and diverticulitis.

NEW ORAL ANTITUMOR DRUG. Uracil-mustard (U-8344), a new oral alkylating agent with a therapeutic spectrum similar to that of other mustard analogues, was given to 130 patients with various neoplastic disorders (J.A.M.A. 174:108, 1960). The drug was particularly effective in treatment of lymphomas and chronic leukemias. Advantages over similar agents are small dosage required, uniform tolerability, simplicity of the regimen. The agent may be of value when other alkylating agents have not been successful.

COD LIVER OIL PROTECTS AGAINST RADIATION. Supplementing the diet of mice with cod liver oil or a starch derivative, dextrin, increased their survival three to six days over controls after exposure to radiation, which normally proves lethal in five days, according to a report to the International Congress on Nutrition. Increased fat stores in the liver may be responsible for the protective effect.

PROTHROMBIN TIME DETERMINATION. A new instrument designed for use with standard "tilt" or "loop" methods provides accurate prothrombin time determinations without the use of a water bath. The device maintains plasma, thromboplastin, and prothrombin pipettes at a constant 98.6 F.; a light source and magnifying viewer assure accurate observation. The instrument is marketed as Thrombitron by Clay-Adams, New York City.

GUIDE TO FETAL DANGER IN PREGNANT DIABETICS. A decline of the estriol excretion level may guide in determining whether a pregnant diabetic patient is in danger of losing her child and should have a cesarean section, according to Ronald Hobkirk (McGill University, Montreal). In a study of 24 such patients, it was found that in those who subsequently had a fetal death, the estriol excretion tended to level off at about 30 weeks, whereas normally the estriol level rises sharply from 30 weeks to the end of pregnancy.

PLANT GROWTH HORMONE STIMULATES CALLUS FORMATION. A plant growth hormone, beta-indoleacetic acid, was shown experimentally to have potential value in callus formation in long bones, according to a report to the International Society of Orthopedic Surgery and Traumatology. The agent, used daily in 3 ml. doses of supersaturated solution and administered by subcutaneous injection, shortened the period required for consolidation of fractures of the long bones in guinea pigs by approximately 14 days. The agent was well tolerated by the animals.

TAKE OF AUTOGRAFTS INCREASED WITH AMNIOTIC FLUIDS. Take of autografts was increased from 33-1/3 to 90 per cent by use of amniotic fluid baths and sprays, according to a report to the French Society of Plastic and Reconstructive Surgery. Donor autografts from the ear lobe were dipped in amniotic fluid before being stitched to various sites on the nose and the grafts were sprayed for several days with a mixture of amniotic fluid and physiological saline. Nine out of 10 patients showed perfect results.

DOG LIVERS SUCCESSFULLY ISOLATED. Livers of 72 dogs were successfully isolated from the blood stream with subsequent return of the organs to normal position without noticeable damage, according to a report at the postgraduate course of the American College of Gastroenterology. The livers were isolated for as long as two hours (in 4 dogs) by use of a specially adapted heart-lung machine. All functions returned to normal when the main blood stream was reintroduced into the livers.

NEW DIURETIC. High potency, long duration, and low toxicity are properties of a new member of the benzothiadiazine family, methyclothiazide (Enduron, Abbott). The oral diuretic is reported to promote greater sodium excretion per unit of potassium excreted and less potassium loss than other benzothiadiazines. The drug may produce a rise in serum uric acid levels; caution is required with patients under treatment with other antihypertensive drugs, particularly ganglionic blocking agents.

Gynecology and Obstetrics in the Old Testament and the Babylonian Talmud*

Part II

Werner Steinberg, M.D.

LINDEN, N. J.

> *"Take ye wives, and beget sons and daughters; and take wives for your sons, and give your daughters to husbands, that they may bear sons and daughters; and multiply ye there, and be not diminished."*
> Jer. 29:6

PREGNANCY

Diagnosis. An existing pregnancy could only be presumed but could not be substantiated until it became evident by the enlarged abdomen. As previously pointed out (part I), an examination by a physician was not permissible "lest women were made repulsive to their husbands" (Yeb. 42a). Therefore, other means had to be employed to establish the diagnosis, one of which was the observation of the woman's gait. Rashi stated that a pregnant woman, walking on soft soil or loose earth, left a deeper impression than a nonpregnant one (Preuss). How successful he was with this type of diagnosis he did not say.

According to rabbinical belief, three sources partake in the creation of man: God, his father, and his mother. The father was thought to supply "the white substance" (semen) out of which were formed the child's bones, sinews, nails, brain substance, and the white of his eyes. From his mother came "the red substance" out of which originated skin, flesh, hair, blood, and the black of his eye, whereas God gave him the breath, the beauty of his features, his eyesight, the power of hearing, speaking, and walking as well as his understanding (Nid. 31a).

Conception. The actual mechanism of conception was shrouded in mystery. Mar Samuel, the physician among the talmudists, had his own opinion, which he expressed as follows: "Any semen that does not shoot forth like an arrow causes no fructification" (Nid. 43a). That implies that any semen not ejaculated could not bring about conception. This statement is so much more remarkable as Ben Sira, the author of the apocryphal book Ecclesiasticus ("Wisdom of Ben Sira"), reported a story that must have been told to him by his mother. According to her account, she conceived him while bathing in a pool in which a man supposedly had had an emission. The possibility of such an accident was acknowledged by the sages (Hag. 15a), and therefore, this was the first time artificial donor insemination was mentioned; more will be said about it (*vide infra*).

The opinion at what age a girl could become pregnant varied from book to book. One story in the aggadic part of the Gemara told of Justinia, the grand-daughter of

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* This is the second part of a three-part article. The complete bibliography will be given after part III.

the Roman Emperor Antoninus Pius (A.D. 138–161), who came to Jehudah ha-Nasi and asked him at what age a girl was capable of conception. "At the age of twelve years and one day" was his answer; "that is where you are wrong," replied the girl. "I got married at the age of six and bore a child when I was seven" (Nid. 45a). The common custom for a girl was not to marry before the twelfth year of age; yet exceptions occurred, and therefore, the rabbis included the marriage of a minor as one of the indications for contraception (part I). The Mishnah recognized that "a girl at the age of three years and one day may be betrothed by intercourse (subject to her father's approval)" (Nid. 44b), a disclosure that is hard to believe. Admittedly, precocious maturity is more common in the Orient than in the Occident; however, the genitals of a 3-year-old girl must be so immature as to make intercourse more painful than pleasurable.

Embryology. Guttmacher, in his afore-mentioned paper (part I), remarked that "Scriptures convey no clear-cut idea of embryology" and quoted a reference from the book of Job: "Hast thou not poured me out as milk and curdled me like cheese? Thou hast clothed me with skin and flesh, and hast knit me with bones and sinews" (10:10, 11).

Similarly, it is reported in the apocryphal book of the Wisdom of Solomon: "The body was formed in the womb of my mother within a time of ten months, curdled in the blood from the male seed and added in the lust of copulation." From this amorphous mass developed a clot (*golem*), which in turn gave rise to the fetus (7:2). In the Talmud, Rabbi Simlai expressed himself thus: "What does an embryo resemble when it is in the bowels of its mother? Folded writing tablets. Its hands rest on its two temples respectively, its two elbows on its two legs and its two heels against its buttocks. Its head lies between its knees, its mouth is closed and its navel is open, and it eats what its mother eats and drinks what its mother drinks, but produces no excrements because otherwise it might kill its mother" (Nid. 30b). This is as exact a description of the intrauterine fetal position that can be found in the Talmud, and it shows a good power of observation; that a fetus urinates into the amniotic fluid was evidently not known.

Contrariwise, the following passage is much more difficult to explain: "During the first three months of pregnancy the embryo occupies the lowest chamber, during the middle ones it occupies the middle chamber and during the last months it occupies the uppermost chamber; and when its time to emerge arrives it turns over and then emerges, and this is the cause of the woman's pains at childbirth" (Nid. 31a). The sages evidently believed that the fetus occupied different "compartments "of the uterus as pregnancy progressed and as the fundus rose cephalad. They also thought that during the greater part of gestation the fetus assumed a breech presentation, which spontaneously converted into a vertex presentation, and that this conversion, not the expulsive forces of the uterus, was the cause of the birth pangs.

Prenatal Care. This term is of a very recent vintage, as the older reader will easily realize. As recently as 40 years ago, a pregnant woman saw her physician only once, in the middle of her pregnancy, to engage him for her confinement, and she did not see him again until she was in labor. Thus, prenatal care existed neither in recent times nor in the Talmudic era. Yet, certain precautions against mishaps

during pregnancy were common knowledge. For instance, coitus was thought to be harmful to mother and baby during the first trimester, whereas during the second trimester, it was believed to be harmful only to the mother, but beneficial to the baby. During the last three months, it was alleged to be beneficial to mother and baby, since it lubricated the birth canal, thus hastening the delivery (Nid. 31a).

Nutrition of the gravida varied considerably from that of her nonpregnant sister. It was customary to keep pregnant women on a soft diet, for a midrashic story reports that God had inquired from Moses, before the exodus from Egypt, whether he had provided "soft food" for the pregnant women and also nuts and cereals for the infants (Exod. Rab. 3:5). From this, one can infer that special foods were cooked for pregnant women depending on their desires and cravings. The Talmudic law gave them also a wide leeway as to the type of food they were allowed to eat; if a woman's pica was directed toward meat that was ordinarily considered *terephah* (i.e., not *kosher*), she was allowed to eat it "because of her serious condition" (Ker. 13a). Since withholding of such food was believed to be injurious to the growing baby, the pregnant woman had a special dispensation in order to preserve it. Some recommended that "barley-gruel," which was held to be easily digestible, be included in a pregnancy diet (Yoma 47a). However, the rabbis cautioned against drinking "Egyptian zithom," a concoction made of a third part barley, a third part safflower, and a third part salt. This mixture was consumed especially between Passover and Pentecost and was supposed to have a salubrious effect on people with digestive trouble; yet, it was said to be dangerous to invalids and pregnant women. Apparently, the potion was too purgative and, therefore, thought capable of provoking abortion (Pes. 42b).

Determination of Sex. The time-worn question, "Doctor, is it going to be a boy or girl?" had already occupied the minds of the Talmudic scholars. They claimed that they could predict the sex from the intensity of the labor pains, which were said to be more severe with a girl than with a boy. Moreover, the sex of the baby also influenced the position of the head during delivery, since it was held that "the female emerges in the position she assumes during intercourse, and the male emerges in the position he assumes during intercourse. The former, therefore, turns her face upwards while the latter need not turn his face" (Nid. 31a). Consequently, according to Talmudic opinion, all female babies were delivered in occiput posterior position.

The Talmud went as far as to teach that one could predetermine, at will, the sex of a baby at the time of coitus. According to the Bible: "And the sons of Ulam were mighty men of valor, archers, and had many sons, and sons' sons, a hundred and fifty" (I Chron. 8:40). This prolific generation of males was explained by the sages as follows: "It is within the power of man to increase the number of sons . . . because they contained themselves during intercourse in order that their wives should emit their semen first so that their children should be males" (Nid. 31b). They evidently assumed that a man who withheld his ejaculation until after his wife's orgasm could, at choice, procreate only boys. In case he was unable to hold out that long, he was to repeat the act.

Duration of Pregnancy and Viability of the Baby. Mar Samuel taught that a normal pregnancy lasted 271, 272, or 273 days. This figure was counted from the first inter-

course of a menstrual cycle, and not from the first day of the last period. As will be shown in part III, the first intercourse did not take place until the eighth day after the end of menstruation, at which time a woman had to take a ritual bath (*mikveh*). Thus, in a woman with a normal 28-day cycle who menstruated four to five days, the first intercourse did not take place until day 12 or 13 of the cycle, which came fairly close to the day of ovulation. The talmudists accepted the accuracy of Mar Samuel's figures of 271 to 273 days and, therefore, recommended intercourse only on a Wednesday, Thursday, Friday, or Saturday so that the onset of labor would not fall on the Sabbath and, thus, lead to its desecration (Nid. 38a).

According to Talmudic sources, the shortest duration of pregnancy that would permit a woman to give birth to a "premature baby" was six months and two days. The proof advanced by the sages was taken from the biblical story of Hannah. Scriptures reported that she conceived after "two cycles and two days"; each cycle (*tekufah*) consists of the fourth part of a year (three months); thus two cycles equaled six months (Nid. 38b).

As to the maximum length of gestation, there existed the same diversity of opinion in antiquity as prevails among modern obstetricians. Most of the rabbis did not believe that a postdate pregnancy was possible, although there is a judicial decision to the contrary in a bastardy suit reported in the Gemara. A woman whose husband had been across the sea for one year was said to have gone three months past the regular gestational period. Raba Tosfa'ah, who heard the case, ruled that such an extended pregnancy was within the realm of the possible and, therefore, declared the child legitimate (Yeb. 80b).

Course of Pregnancy. The as yet insufficiently explained miracle of a baby's growth in the uterus was duly recognized and marveled at by the sages. They could not understand why a child carried in an "upside-down" position in the uterus would not "fall out" of its container, just "like coins would fall out from a purse turned upside-down," except through an act of God. By the same token, they could not comprehend why a man who spent an hour in a hot temperature would hardly survive, whereas "the child lay within the boiling inwards of the woman, yet stayed" (Lev. Rab. Par. 14).

The rabbis attributed the pangs that women had to endure during pregnancy and labor to Eve's original sin in the Garden of Eden when God disclosed the penalty for her transgressions: "I will greatly multiply thy pain and thy travail; in pain thou shalt bring forth children" (Gen. 3:16). According to Talmudic thought, only the righteous woman was excepted from this decree, for it is reported of Jochebed, the mother of Moses, that, because of her God-fearing life, her childbearing was painless (Sot. 12a). Certain privileges to the gravida were denied to her nonpregnant sister. The pica of pregnancy was regarded as a natural phenomenon accompanying gestation against which the woman should not resist. Therefore, on the highest holiday of the Jewish religion, the Day of Atonement, when the Jew is required to fast for 24 hours to repent his sins, the woman with child is allowed to eat "so as not to starve her unborn babe." Teaches the Mishnah: "If a woman with child on Yom Kippur smelt a dish and has a morbid desire for it, she must be given to eat until she feels restored. A sick person is fed at the word of experts (physicians)" (Yoma 82a).

The pica of pregnancy was thought to originate with the fetus and not with the mother; thus, the sages concluded, if a pregnant woman could resist the desire for certain foods, it was because of the piety of the fetus and not the will power of the mother.

Similarly, fetal movements were explained as expressions of the unborn child's mood, for a fetus led his own life before birth. For instance, the Midrash tells that, while Rebekah was pregnant with Jacob and Esau, each time she passed a synagogue, Jacob began to stir in the uterus; however, when she passed a temple of an idol, Esau started to move around. The violent intrauterine kicking of the twins caused their mother much pain and discomfort and she inquired among her neighbors whether they had had a similar experience. The unabated fetal movements must have robbed Rebekah of much of her sleep, because in a moment of utter disgust she exclaimed that she would rather not have become pregnant at all than to endure the constant torment (Midr. Rab. Gen. 63).

Vagitus uterinus, a phenomenon generally accepted nowadays, was viewed with skepticism by the talmudists. Someone once told Raba: "I heard the child cry late on the Sabbath eve, but it was not born until the Sabbath." To this Raba replied: "This is a case of a child whose cry could be heard and who put his head out of the ante-chamber [vulva] on the Friday night." Raba evidently did not give credence to the story for he believed that crying could take place only when the head had actually been born; therefore, he ordered that the circumcision was to take place before the onset of the Sabbath instead of afterward (Nid. 42b).

Fetal Development. There existed a wide variation of opinions as to which organ of the body was first formed. Some thought that the head was the original part of the baby fashioned, whereas others made the navel the core of formation whence the rest of the body developed in a centrifugal manner, while still others regarded the nose as the source of existence, because it is said: "In whose nostrils was the breath of the spirit of life" (Sot. 45b). The sages evidently realized that the embryo was nourished through the umbilical cord and that the free flow of blood through it was indispensable for the maintenance of life. In the midrashic commentary to the Song of Songs, we are told of a metaphor in which the umbilicus is likened to the synhedria of the Jews: just as the babe in the uterus receives its nourishment through the navel, so do the Israelites derive the inspiration necessary for their cultural existence from their high courts (Cant. Rab. 5:3).

An old superstition, which can be traced back as far as Hippocrates, held that an 8 month baby had less chance of survival than one born after 7 months' gestation. According to Zimmels, it was thought that "a child born in the seventh month has a greater warmth and moisture, and therefore, its complete formation took less time than a nine month baby which was completed only after that time; birth within the eighth month is not natural." Rabbi Abbahu compared an 8 month baby to a stone since it was thought to be nonviable. Rabbi Jehuda defined such a fetus as one whose hair and nails were not developed. He then continued: "The reason then is because they were not developed, but had they been developed it would have been assumed that the child was a seven month one, only his birth was somewhat delayed" (Yeb. 80b). This erroneous belief has remained in the literature down into the Middle

Ages, and it was only recently realized that the survival rate depended more on the birth weight than on the length of gestation.

Animation of the Body. Antoninus,* a friend of Rabbi Jehudah ha-Nasi, has often been mentioned in the Talmud. One of their conversations deals with their opinion about the exact time the soul enters the body: whether this occurred at the time of conception or at the time the body was formed. The rabbi stated: "At the time of formation." Thereupon the questioner rejoined: "Can a piece of meat be unsalted for three days without becoming putrid?" By this Antoninus implied that if the sperm cell were not immediately endowed with a soul, it would become putrid, and then could not fertilize the ovum (I. Epstein, Sanh. 91b). The question as to the time of animation of the body never had any immediate significance in Jewish thinking; however, it became of paramount importance in Christian theology.

Superfetation. As was pointed out in the section "Talmudic Attitude Toward Contraception" (part I), superfetation was held quite possible by the talmudists; for fear of such a mishap, they permitted a pregnant woman to use a contraceptive tampon so that a new pregnancy would not compress the growing fetus and make a *sandal* out of it. To cite an example of superfetation, the Gemara reports a somewhat humorous story: "It once happened that a child was born three months later than its predecessor and lo, both sit before us in the schoolhouse. And who are they? Judah and Hezekiah, the sons of Rabbi Hiyya. But did not a Master say that a woman in conception cannot conceive again? Abaye replied: 'It was the same drop but it was divided in two sections; the features of one were completed at the beginning of the seventh month and those of the other were completed at the end of the ninth month' " (Nid. 27a).

Duration of Female Procreative Power. The Bible abounds with stories of postmenopausal women getting pregnant and delivering babies, an example of which is the tale of Sarah. According to the Scriptures, she was "old and well stricken in age; and it ceased to be with Sarah after the manner of women" (Gen. 18:11). Even if one discounts the discrepancy between the Biblical and the Gregorian year, one still cannot reconcile the fact that Abraham was 100 years old when he begat Isaac. Of Sarah, whose breasts exhibited menopausal atrophy, it is reported that "they opened up like wells" so that she was able to nurse not only her own child but those of her visitors as well (Gen. Rab. Par. 53, 5:7). The Talmud tries to explain the fact that Sarah conceived after having entered the menopause by assuming that she had miraculously resumed menstruation (Bab. Mets. 87a).

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* The Talmud does not make it quite clear who Antoninus really was. Like royalty nowadays, the Roman emperors were given from five to eight names, and some of them appeared over and over. To avoid confusion, the name by which they became known in history had to differ from that of their predecessor. For instance, the full name of Emperor Tiberius (A.D. 14–37) was Tiberius Claudius Nero, that of his nephew Claudius (A.D. 41–54) was Tiberius Claudius Drusus, who in turn adopted Nero (A.D. 54–68), whose real name was Claudius Nero. Thus, the aforementioned Antoninus may have been the Emperor Antoninus Pius (138–161), who gained fame in Jewish history when he abrogated the infamous hadrianic laws and restored the freedom of the Jews to practice their religion according to their tradition. Others thought that it was the Emperor Marcus Aurelius (161–180), who likewise carried the praenomen Antoninus (Braunschweiger), and finally, the *Standard Jewish Encyclopedia* speculates that the Antoninus in question in reality was the later Emperor Caracalla, who was born in 176, but did not begin his reign until A.D. 211.

The story of Jochebed, the mother of Moses, was likewise explained through a miracle. According to Talmudic sources, she was 130 years old (Sot. 12a); yet it is reported "that marks of youth re-appeared on her. The flesh of her body was again smooth, the wrinkles of old age were straightened out and her beauty returned" (Bab. Bath. 120a).

Artificial Insemination. The previously cited tale that Ben Sira told about his mother having conceived while taking a bath cannot be called, strictly speaking, artificial insemination; as Kleegman correctly pointed out, the former conception occurred accidently, whereas therapeutic insemination, as practiced by physicians today, is "intentional" to alleviate childlessness of a married couple. Besides the Talmudic quotation (Hag. 15a) on which Ben Sira based his own story, the "possibility of such generation *sine concubito*" (Jakobovits) has been related by the twelfth-century Arabic physician Averröes in his treatise *kitab el kollijjat* (Preuss). It later was reiterated by the Marrano physician Amatus Lusitanus, who used it in the defense of a nun who had aborted a hydatidiform mole to clear her from the suspicion of fornication (Friedenwald).

In modern times the method has not found approval from either Catholic or Jewish clergy, and it has therefore been condemned by both with equal fervor. According to Jakobovits, the first Roman Catholic statement denouncing artificial insemination was made in a Holy Office decree in 1897. Ever since, the Church has rejected this practice, irrespective of whether the semen was supplied by the husband or by a donor. This view was restated by the late Pope Pius XII in an address to the Second International Congress on Fertility and Sterility, held in Naples in 1956. The Pontiff reproved this type of treatment for two basic reasons: first, because of the means by which the semen was obtained (by masturbation or coitus interruptus) and, second, "because it violated the natural law and was contrary to law and morality."

Jakobovits has collected a number of modern rabbinical pronouncements on this subject. He cited a *responsum* of a Budapest rabbi in 1930 who held that artificial insemination by donor was to be looked on as "plain adultery" and "the children so produced as *mamzerim*" (a child born from an incestuous union prohibited under penalty of death). Although later opinions were less stringent, nevertheless the opposition of the contemporary orthodox rabbinate has been just as unequivocal. "The principal motives for the revulsion against the practice is the fear of the abuses to which its legalization would lead, however great the benefits may be in individual cases. By reducing human generation to stud farming methods, A.I.D. severs the link between the procreation of children and marriage, indispensable to the maintenance of the family as the most basic and sacred unit of human society" (*loc. cit.*).

Orthodox Judaism had, by necessity, to reject artificial insemination by donor for reasons of religious laws. According to Mosaic command, "if brethren dwell together, and one of them die, and have no child, . . . the husband's brother shall go in unto her, and take her to him to wife" (Deut. 25:5). This so-called "levirate marriage" had as its motives the preservation of the family's property right in the widow as well as the raising up of seed for the deceased brother (L. M. Epstein). Thus, in case of a successful artificial insemination, the deceased brother had not sired

the child, and therefore, the levirate duty would still be in force notwithstanding the fact that the woman had a child born during the marriage. Likewise, the priesthood title of a *Cohen* was considered hereditary; would then the son of a priest conceived through artificial insemination by donor be entitled to the office of his father? These were important questions in the life of the orthodox Jew, and therefore, it is little wonder that orthodox rabbis have come out so unconditionally against artificial insemination by donor.

As Jakobovits denoted, the attitude changed when it came to the question of artificial insemination by husband. The majority of orthodox rabbis were willing to permit this form of conception, except for the method by which the semen was obtained. Since "the bringing forth of semen for no purpose" was strictly forbidden (see part I), the ejaculate would have to be obtained in some other way to be acceptable.

LABOR AND DELIVERY

The approaching labor is well described by the prophet Isaiah: "A woman with child, that draweth near the time of her delivery, is in pain (*tahil*) and crieth out in her pangs" (Isa. 26:17). If one studies the etymology of the word *tahil*, one finds it derived from *hul*, meaning "to whirl, dance, writhe," which depicts the actual twisting of the body of the woman in severe labor pain. Thus, the wailing and lamenting was accepted as a normal reaction of impending labor.

The position that a woman of Biblical and Talmudic times assumed to bear her children has given rise to much controversial comment. The Bible tells us of the daughter-in-law of the prophet Eli, the wife of Phinehas, who, on hearing the bad tidings of the death of her husband and father-in-law, "bowed herself" or "knelt down" (*vatikhra*) and brought forth (I Sam. 4:19). The word *kara* usually denotes the position one assumes in kneeling down to drink from a fountain as well as to worship. The Talmudic sages expounded on this sentence: "When a woman kneels down to give birth, she presses her heels against her thighs and thus gives birth" (Yeb. 103a). In all probability, the parturient woman knelt (squatted) between the thighs of her attendant, which can be regarded as the most natural position of primitive peoples (see Gen. 30:39, 50:23). In postbiblical times, this must have changed, since Mishnah as well as Gemara speak of a "birth-stool" (*mashber*) on which the woman sat as soon as her labor pains began. In Biblical Hebrew *mashber* means "mouth of the womb" (Gesenius), which has been preserved in the new Hebrew. However, in Talmudic Aramaic the word is met with on several occasions (such as Kel. 23:4 or Arak. 7a) and can only be understood to represent a chair or stool on which the parturient woman remained during her entire labor. Soranus gave an exact description of such a "midwife's stool" (Temkin), and this brings up the question of whether the Hellenistic influence had introduced this appurtenance in Judea or vice versa.

Much more difficult is the interpretation of the word *obnayim*, which is said to be synonymous with *mashber* and which appears in the Bible twice. Once, it is used by the prophet Jeremiah in his story of the potter and his clay: "Then I went down to the potter's house, and, behold, he was at his work on the wheels (*obnayim*)"

(18:3) (*vide infra*). In this connection, the translation of "potter's wheel" is the only one possible. The second time the word is mentioned is in Exodus: "And the king of Egypt spoke to the Hebrew midwives, . . .: When ye do the office of a midwife to the Hebrew women, ye shall look upon the *obnayim*: if it be a son, then ye shall kill him; but if it be a daughter, then she shall live" (1:15, 16). In this context, the term *obnayim* is variously translated as "birthstool" (Gesenius) or "passage of the embryo, vagina" (Jastrow). The Talmud offers still another explanation: "What means *obnayim*? Rabbi Hanan said: 'He entrusted them with an important sign and told them that when a woman bends to deliver a child, her thighs grow cold like stones (*abanim*).' Another explains the word *obnayim* in accordance with what is written: 'Then I went down to the potter's house, and, behold, he wrought his work on the wheels.' As in the case of the potter, there is a thigh on one side, a thigh on the other side and the wooden block in between, so also with the woman is a thigh on one side, a thigh on the other side and the child in between" (Sot. 11b). Finally, the Midrash has a fourth interpretation: "The womb bears this name, because there the child originates; or because God lets the thighs of the travailing woman get as hard as stones, for else she must die" (Exod. Rab. Par. 1, Ch. 5:16). Thus the real meaning of the word *obnayim* remains a moot point.

The Bible tells us that Hebrew women show a particular eutocia; according to the Egyptian midwives "they are lively" and usually have precipitous deliveries before the midwife gets to them (Exod. 1:19). That this was not true of all Jewesses will be shown from the delivery stories.

The definition of what constitutes labor differs substantially from our modern conception. Whereas we associate the term "labor" with a progressing dilatation of the cervix and descent of the head, the sages took the appearance and disappearance of pains as the only criterion of labor. Thus, protracted labor may continue for 40 or 50 days (Nid. 36b). The blood emitted while the pains last is Pentateuchically clean, whereas that discharged during cessation of pains is considered like menstrual blood, and thus unclean. Therefore, if there had been bleeding during a pain remission, it was considered to be menstrual blood and the woman came under the same restrictions as during menstruation.

Delivery Stories in the Bible. There are five delivery stories to be found in the Bible, two of which concern twin births, whereas the other three end in the demise of the mother. Three of these women were attended by midwives; in the remaining 2 cases, no attendant is mentioned although one may conjecture that in the case of Rebekah, there might have also been a midwife in attendance, since Isaac undoubtedly had the means to provide his wife with such luxury.

Rebekah. "And when her days to be delivered were fulfilled, behold, there were twins in her womb. And the first came forth ruddy, all over like a hairy mantle; and they called his name Esau. And after that came forth his brother, and his hand had hold on Esau's heel; and his name was called Jacob" (Gen. 25:24–26).

Rebekah must have suspected beforehand the impending multiple birth, for the Scriptures report: "the children struggled within her." The "hairy mantle" that is ascribed to Esau was a hypertrichosis, although the color of his hair is not entirely

clear. *Admoni* is variously translated as "ruddy" or "gold-colored" or blond, which probably refers to the color of his hair and not that of his skin. The twins, because of their dissimilarity, must have been dichorionic (fraternal), thus occupying two different chorionic sacs. We may assume that, after the delivery of the first twin, the membranes of the second sac ruptured, thus allowing the prolapse of one hand, which accounts for the statement that Jacob held on to Esau's heel. Otherwise, we have no details about this delivery.

TAMAR. "And it came to pass in the time of her travail, that, behold, twins were in her womb. And it came to pass, when she travailed, that one put out a hand; and a midwife took and bound upon his hand a scarlet thread, saying: 'This came out first.' And it came to pass, as he drew back his hand, that, behold, his brother came out; and she said: 'Wherefore hast thou made a breach for yourself?' Therefore his name was called Perez. And afterward came out his brother, that had the scarlet thread upon his hand; and his name was called Zerah" (Gen. 38:27–30).

This passage tells us of the twins that arose out of the incestuous union of Juda, the son of Jacob, and his daughter-in-law Tamar. Obstetrically, the story has a number of connotations. According to Preuss, the course of the delivery was explained by Winckel (*Handbuch der Geburtshilfe*) thus: Both babies were in vertex presentation. The arm of one prolapsed alongside the head of the other, but was pushed aside by the advancing head of the second baby. Later the arm probably appeared together with the appropriate head (compound presentation) after the canal was dilated. This sequence of events appears to be more credible than another likewise advanced by Preuss: The first baby was in a shoulder presentation when one arm prolapsed. Then the second twin descended, making the first one with his prolapsed hand recede into the uterus, whereupon the second twin was born; afterward the first twin was expelled. Thus, the presentation of the first twin was spontaneously converted from oblique to vertex or the baby was born *conduplicato corpore*. This concept would become more acceptable if one presumed with the Talmud that Tamar's delivery took place before the normal end of the pregnancy, making both babies premature. The talmudists deduce this from the text: in the case of Rebekah, the Scriptures state that her days to be delivered were fulfilled, whereas they report of Tamar simply, "at the time of her travail," without giving details as to the time of her gestation. It remains very debatable whether any of these explanations are tenable, and Miller observed rightly that "this is, as far as I know, the only instance in all literature of twins in which such a sequence in the birth of the two children is recorded."

The midwife attending Tamar's delivery and her diagnostic acumen in predicting the twin birth were mentioned previously (part I). It bespeaks the wealth of her father-in-law (and father of the baby) that he obtained the services of a midwife to supervise the parturition, which otherwise was attended only by nontrained neighbor women. The midwife employed a scarlet thread, which may be compared to our modern identification bracelet, to ensure Zerah's firstling right, which, according to Talmudic jurisprudence, entitled him to certain privileges. To safeguard them, it sometimes became necessary to obtain the midwife's testimony, one of the few cases where a woman's testimony was admitted in court (Kid. 74a).

RACHEL. "And they journeyed from Beth-El; and there was still some way to Ephrat; and Rachel travailed and she had a hard labor (*vatekash*). And it came to pass, when she was in hard labor (*hakoshetah*), that a midwife said to her: 'Fear not, for this is also a son for thee.' And it came to pass, as her soul was departing (for she died) that she called his name Ben-oni." (Gen. 35:16).

This is the first of three narratives that ended in a maternal fatality. One cannot help but feel a deep compassion for this unfortunate woman, for Rachel was actually the only one of Jacob's four wives whom he deeply loved and for whose hand he had toiled 14 long years. When he finally was able to take her home as his wife, she remained barren for the first years of her marriage (part I). After a period of long waiting, she conceived Joseph whom, according to the Bible, she bore without any difficulties. Preuss stated that the time interval between Joseph and Benjamin was about 10 years, so that Rachel suffered not only from a primary, but also from a secondary sterility.

The terms *vatekash* and *hakoshetah* are both derived from the verb *kashah*, which means both, "to have a hard time" as well as "to become hard"; thus it is possible that the text wanted to imply that Rachel's hard labor was due to a hardening of the uterus such as seen in dystocia and that her death was caused by tetanic contractions causing rupture of the uterus and postpartum shock. The dystocia must have resulted from a cephalopelvic (or, more correctly, sacropelvic) dysproportion because we are told that the midwife was able to predict the sex of the baby before it was born; this lets one assume that the baby was in breech presentation.

The phrase "as her soul was departing" indicates that Rachel did not lapse into unconsciousness, for she was able to call her son by a name that was close to her Aramaic mother tongue, Ben-oni, son of my sorrow, which Jacob later changed to the Hebrew Benjamin. Thus, the cause of her death could also have been a postpartum hemorrhage or possibly a cardiac failure. Rabbi Hertz commented that, strangely enough, the Bible does not mention Jacob's grief, which must have been profound, and only 13 chapters later do we find a small reference documenting the patriarch's feelings: "And as for me, when I came from Paddan, Rachel died unto me in the land of Canaan on the way, when there was still some way to come to Ephrat; and I buried her there on the way to Ephrat—the same is Bethlehem" (Gen. 48:7). Still today, Rachel's tomb is visited by travelers going from Jerusalem to Bethlehem, thereby crossing the border into Jordan on the outskirts of Bethlehem. Of this grave sings the prophet: "A voice is heard in Ramah, lamentation, and bitter weeping, Rachel weeping for her children; she refuseth to be comforted for her children, because they are not" (Jer. 31:14).

PHINEHAS' WIFE. "And Eli's daughter-in-law, Phinehas' wife, was with child, near to be delivered; and when she heard the tidings that the ark of God was taken, and that her father-in-law and her husband were dead, she bowed herself down and brought forth; for her pains came suddenly upon her. And about the time of her death the women that stood by her said unto her: 'Fear not, for thou hast brought forth a son.' But she answered not, neither did she regard it. And she named the child Ichabod, saying the glory is departed from Israel" (I Sam. 4:19–22).

The Talmud mentions in connection with this story a poorly understood play on

words. The term the Bible uses for "labor-pains," *tzireha*, literally means "her hinges"; thus the Talmudic scholars comment: "As a house has hinges, so a woman's body has hinges in her sexual organ (uterus)" (Bek. 45a). Exactly how they meant this is not clear.

The Book of Samuel gives fright as the cause of the onset of labor, a fact well known and often observed; any emotional upheaval brings about a chain of events in the pituitary-adrenal axis, which finally may lead to uterine contractions. As to the ultimate cause of her death, the Scriptures remain silent.

MICHAL. "And Michal the daughter of Saul had no child until the day of her death" (II Sam. 6:23). This is the only sentence about the tragic fate of Saul's daughter, who was married to David. According to the Midrash, Michal did not have a child until the day of her death, but she did have one on that day (I Chron. 3:3). "Why is Michal called here *eglah*? Because she lowed like a calf (*eglah*) and died" (Gen. Rabba Par. 82, 5:16). The Talmud takes a somewhat different view. "Rab. said: Eglah is Michal. And why was she called eglah? Because she was beloved by him, as an eglah by its mother." Rabbi Hisda interpreted the sentence, "she had no child until the day of her death," to mean that she actually died in childbirth (San. 21a). Michal apparently became pregnant after years of sterility, and Goldschmidt explained that David's estrangement, rather than divine punishment, was the cause of her barrenness. Otherwise, we know no other details about this third and last of the maternal deaths.

PUERPERIUM

Lying-In Period. Superstitions and misgivings have governed the disposal of the placenta from biblical down to modern times. The placenta had to be buried in the ground lest some evil event befall the newborn babe. The Hebrew word for the placenta is *shilyah*, which is once mentioned in the Bible (Deut. 28:57) and then is found several times in the Talmud, *viz.*, "The placenta in its first stage resembles a thread of the woof and in its final stage it resembles a lupine. It is hollow like a trumpet, and no placenta is smaller than a handbreadth." Rabbi Simeon ben Gamaliel stated: "The placenta resembles the craw of a hen out of which the small bowels issue" (Nid. 26a). The presence of a placenta rendered a house unclean because there can be no placenta without a child. However, Rabbi Simeon agreed "that the child may have been mashed before it came forth" (*ibid.*) and that an amniotic sac without a fetus might have been expelled. Thus the concept of the "blighted ovum" was already known to the talmudists. The disposal of the placenta was subject to certain rules and regulations. First, it was put into a bowl and carried to an anteroom (Nid. 27a), since the house became unclean if the placenta were within its walls. It then was buried outside, but must not "be buried at cross-roads or hung on a tree, for these are Amorite practices" (Hul. 77a).

The time one has to wait for expulsion of a placenta after delivery is 10 days (Nid. 27a); else one may expect the presence of a second baby. Manual removal such as was practiced by Soranus (Temkin) and Aëtius (Findley) was unknown to the Talmudic physicians. Some of the superstitions of the folklore of neighboring peoples

found their way into the Talmud; Rabbi Abaye related a story told to him by his mother: "If an infant does not breathe easily, his mother's after-birth should be brought and rubbed over him, and he will breathe easily. Or if it is too thin, his mother's after-birth should be rubbed over him from its narrow end to its wide end, if it is too fat it should be rubbed vice versa" (Shab. 134a).

Suckling by Mother or Wet Nurse. Suckling one's baby was a holy task of every mother and counted as one of the duties that a husband could expect from his wife (Keth. 59b). He actually could compel her to perform this chore or else he could divorce her. Breast-feeding was to be continued for 24 months; after that, it was regarded as an abominable thing (Keth. 60a). If the mother became widowed during that time, she could not remarry before she had discharged this maternal duty.

Spontaneous leakage of human milk rendered clothes or articles unclean, "because the blood issuing from her wound is unclean" (Maksh. VIII). Evidently, the sages believed that during pregnancy "the menstrual blood is decomposed and turns into milk" (Nid. 9a), which accounts for the uncleanness. This same idea was taught by Hippocrates when he said: "If a woman is neither pregnant nor has given birth produce milk, her menstruation has stopped" (Aphorisms 39).

As mentioned in part I, the nursing woman belongs in the category of those who are permitted to use a contraceptive tampon. The reason for this is given: "If the woman conceive while nursing, her milk would become turbid, and she might thereby cause the death of the child" (Yeb. 42b). The sages also recognized the danger for the mother, should her breasts become engorged, for they feared serious illness arising out of stagnated milk (Tos. Shab. XVI).

The superstition that a nursing woman was unable to conceive because she was amenorrheic was already prevalent in Biblical times. Thus, the prophet Hosea tells us that his wife could not conceive until she had weaned her daughter Loruhamah, whereafter she became pregnant again and bore a son (Hos. 1:8).

Breast-feeding was held of such unequivocal importance to the baby's welfare that a wet nurse (*meneketh*) was hired for the entire two-year period whenever a mother was unable to suckle her baby. Whether the wet nurse had to be a Jewish woman or whether she could belong to a "heathen" people was differently decided by various rabbis. When the infant Moses was found by Pharaoh's daughter, Moses' sister Miriam said to her: "Shall I go and call thee a nurse of the Hebrew women?" (Exod. 2:7). Comments the Talmud: "Why just of the Hebrew women? . . . He said, 'Shall a mouth which will speak to the Divine Presence suck what is unclean?' " (Sot. 12b). These rabbis undoubtedly felt that a Jewish baby became "contaminated" if breast-fed by a non-Jewess, and therefore they preferred a Jewish wet nurse. This attitude does not prevail in other books of the Gemara. For instance, Rabbi Johanan ruled that an infant may be "breast fed by an idolatress or an unclean beast, and there is no need to have scruples about his sucking from a detestable thing" (Yeb. 114a).

This is but another example of the tolerance of Jewish theological thinking. The great number of Mosaic laws are completely superseded by the all-important *pikuah nefesh*, which literally means "removing a person from under debris" and then came to connote generally "saving an endangered life" (Jastrow). Thus the preservation

of life outweighs all other precepts concerning the Sabbath or even the holiest of all days, Yom Kippur. Exclaims the Talmud: "There is nothing that comes before the saving of life except three things: idolatry, incest and blood shed" (Ket. 19a). As will be shown in the chapter on embryotomy, the Jews have always held that preservation of an existing life (which does not begin until after birth) is one of the most important *mitzvoth* (religious duties) of any physician.

TERATOLOGY

The congenital malformations mentioned in the Scriptures may be subdivided into two groups: those that are incompatible with life (*sandals* and monsters) and those that will not impair viability (*tumtums*, hermaphrodites, *aylonithş*, and *saris*). The question had, in Talmudic times, an immense practical significance, because of the law of uncleanness (*niddah*), which will be dealt with in part III. If, for instance, a woman passed a blood clot not containing parts of a conceptus, she was subject only to the uncleanness of menstruation (seven days), but if the "clot" was part of a pregnancy, thus a miscarriage, the duration of her uncleanness was 40 to 80 days, depending on the sex of the aborted fetus (Nid. 21a). Although some rabbis may have in private admitted that an abortion may have "the shape of a beast, a wild animal or a bird," Rabbi Meir ruled in the name of the majority: "Anything that has not the shape of a human being cannot be regarded as a human child" (*loc. cit.*).

Sandals. The term *sandal* was already referred to in part I, when it was shown that a pregnant woman was permitted to use a contraceptive tampon lest her fetus degenerate into a *sandal* (*fetus papyraceus* or *compressus*). The literal meaning of the word is "flat-fish," such as sole or turbot. At first, the fetus develops in a normal fashion, but later "dies and is crushed." Thus, a *sandal* can occur only in a twin pregnancy, and according to Talmudic law, it must have facial features, "even if the head appeared twisted backward similar to that of a man who slapped his fellow and caused his face to turn backwards" (Nid. 25b). The delivery may take place per vaginam or it may be that the full-grown fetus is delivered by "cesarean section" (*vide infra*) and the *sandal* through the vagina (Nid. 26a).

Monsters. It stands to reason that the various malformations encountered today were already known to the Talmudic physicians; yet, while we usually give them descriptive names (anencephalus, monobrachius, sympus monopus), the rabbis tried to compare them to some known form of their environment, thus employing sometimes rather poetic names. This makes their identification sometimes difficult. Besides that, there has been no unanimity among the sages as to what constitutes a malformed baby. According to Rab, an infant was regarded as "human" if its face was that of a human being, but the body that of a he goat; in the reversed case, however, it was not declared a "valid birth." Rabbi Jeremiah ben Abba taught that the forehead, eyebrows, cheeks, and chin must all be present to declare it a "valid birth." If these organs could be differentiated on a baby, the definition "features of a human face" was satisfied (Nid. 23b).

A fetus described as "with one eye and one thigh" undoubtedly is a cyclops with a spontaneous amputation of one leg. A baby born with a "perforated gullet"

would present an external esophageal fistula, which according to Potter is very unusual. A "stumped body" would correspond to an amelus, a monster without any extremities. If an animal was born with its haunch and abdominal hollow missing, it was like carrion. When Rabbi Giddal spoke of a *gulgoleth atumah*, i.e., an embryo whose skull is a shapeless lump or on whom no skull is discernible, one is certain that he meant an anencephalus. The same sage spoke of an *aphketah dediklah*, which actually means the ramified portion of the palm leaf. This, applied to an embryo, calls to mind the sirenomelus formation (Nid. 24a). A divergence of opinions existed as to whether a fetus with two backs and two spinal columns was considered a "valid birth," as proposed by the physician Mar Samuel. Doubtlessly, he was referring to conjoined twins, i.e., some type of pagus formation (Nid. 24b).

Far more difficult is the interpretation of two terms, *panav musmasin* (mashed face) and *panav tuhoth* (face covered over). The former term is derived from the verb *masmes*, meaning "to press, to squeeze," and is used in a different connection to describe "flesh in a state of dissolution or liquefaction" (Hul. 45b). Thus, one would be entitled to translate this expression with "macerated face." *Tuhoth* can be etymologized from *tuah* meaning "to cover with a cohesive substance, to plaster," thus implying that the face was covered with something making detailed features indistinguishable. This makes one think of either a baby born under a caul or possibly the expulsion of an amniotic sac containing a missed abortion. Nevertheless, these embryos still have some similarity to existing creatures. However, when Rabbi Jehuda likened a fetus to a *lilith*, he was clearly entering the territory of legend. According to an Oriental fairy tale, a *lilith* was a kind of "female night-demon which has long hair [Erub. 100b], wings [Nid. 24b], and waylays by night children and kills them" (Levy, vol. II, 501). Remarks the Talmud: "If an abortion had the likeness of a *lilith* its mother is unclean by reason of its birth, for it is a child, but it has wings" (Nid. 24b). The same held true if an abortion had the likeness of a serpent, which was considered a valid birth, "since its eye-ball is round like that of a human being" (*ibid.*).

Sexless and Bisexual Children.

Tumtums. The root of the noun *tumtum* originates from the verb *timtem* meaning "to plug up, to obstruct, to knead"; thus, a *tumtum* is a creature whose genitals are covered by a membrane and thus hidden, and therefore its real sex cannot immediately be decided.* Potter, in describing this type of malformation, declared: "The urethral orifice is located at the junction of the penis and scrotum. With such severe defect the corpora cavernosa are frequently smaller than normal and the penis is reduced, sometimes being mistaken for a hypertrophied clitoris, especially if the region of median raphe of the scrotum is indented and the scrotum bilobate. The two parts of the scrotum are often interpreted as labia associated with absence of the vagina." The *tumtum* may exhibit a "dorsal slit," thus establishing his gender as a male (Tos. Yeb. XI, 1), and then, of course, he may marry a woman. Such a condition was described by Rabbi Jehuda, who told of "the *tumtum* of Bairi who, after having been placed upon the operating table and operated upon, begat seven children."

* The most appropriate translation corresponding to modern terminology would be hypospadias.

(Yeb. 83b). The doubtful sex of the *tumtum* is attested by the Talmudic statement that it might be subject either to a penile discharge (gonorrhea) or to bloody discharge (menstruation) (Zab. II, 1). The final decision of whether a *tumtum* was to be regarded as male or female depended on its urination. If urine issued from the male part, it was regarded as a male, and vice versa (Bek. 42b). Because of its doubtful sex, a marriage "either to a husband or to a wife is of doubtful validity and requires a divorce because of the doubt" (L. M. Epstein).

HERMAPHRODITES. Whereas the etymology of the Aramaic word *tumtum* went back to biblical Hebrew, the term *androgynos* was borrowed from the Greek. It means "man-woman" or, in modern terminology, "hermaphrodite." In the case of the *tumtum*, the genitals were hidden, and for that reason, it was of an ambiguous sex; the *androgynos* displayed manifestations of male and female genitals and, therefore, belonged in a special category of creatures, being different in its medical, judicial, and religious aspects. As a firstborn, neither it nor the *tumtum*, received the double portion of the inheritance nor did it share in the rest like its brothers (Bab. Bath. 140b). The Mishnah explains in detail some of the rights and duties of the *androgynos*: "He is in some things like to men, in other things like to women, in other things again he is like to men and to women, and in others he is like to neither men nor women. Wherein is he like to men? He contaminates with the seminal flux like men, and he dresses like men. He can take a wife but cannot be taken *as* a wife like men. At his birth his mother must count the blood of purification like men, and he must not be alone in the company of women like men. . . . And wherein is he like women? In that he contaminates with his menstrual flow like women; and he must not be alone in the company of men like women. . . . At his birth his mother remains unclean on account of the blood of her impurity; and like women, too he is disqualified from acting as a witness. . . . Wherein is he compared to both men and women? . . . His mother must at birth bring an offering as for men and women. And wherein is he likened neither to men nor to women? No penalty is incurred by him on entering the Temple in an unclean state." Rabbi Jose said: "The hermaphrodite is a creature by itself, and the sages could not decide about him. But this is not so with one of doubtful sex (*tumtum*), for such a one is, at times, a man and at others, a woman" (Bik. IV, 1 *ff.*).

THERAPEUTIC ABORTION AND EMBRYOTOMY

Interruption of Early Pregnancy. Although the topic of abortion is to be dealt with in part III, since it is immediately related to the laws governing "menstrual impurity," it is necessary to define here a few Talmudic terms. The word most frequently used for an aborted conceptus is *nefel*, which is derived from the verb *nafal*, meaning "to fall, to be dropped"; thus the expression, which is employed to signify the viable, term, or near-term fetus, is not used for an aborted embryo. The latter just "falls out" or "is dropped." Of it the Psalter declares: "Let them be as a snail which melteth and passeth away; like the untimely births (*nefel*) of a woman, that have not seen the sun" (Ps. 58:9). The same meaning is found in a reference of the book of Job: "Or as a hidden untimely birth I had not been; as infants that never

saw the light" (3:16). In this meaning, the noun *nefel* is also detected on several occasions in the *masekhta* Niddah; yet, on others, it has an entirely different connotation: "Rabbi Simeon ben Gamaliel said: 'Any human being who lives thirty days is not a *nefel*,' because it is said 'And those that are to be redeemed of them from a month old shalt thou redeem' " (Shab. 135b). According to this interpretation, a premature baby that lived less than 30 days was counted as a *nefel*. *Mutatis mutandis*, we read in Exodus: "If men strive together, and hurt a woman with child, so that her fruit (*yeladeha*) depart . . ." (21:22). In this context, the Scriptures use the term *yeled* (child) synonymous with an expelled abortion, a word taken up by the Mishnah, where the judicial significance of the Biblical sentence is discussed (Bab. Kam. V, 4).

If the Talmud wishes to imply that an intact ovum, i.e., the unruptured chorioamniotic sac, was expelled, the word *shefir* (membranous bag) is used; it can be filled either with water or with blood or with fibers. One rabbi even claimed to have seen a *shefir*, which consisted of a sac containing a calf's embryo of the size of a bean (Talm. Yerush. Naz. VII, 56b).

A third term deserves mentioning, namely the word *ruah*, which actually means "wind or spirit." Preuss translated it into German as *Windei*, a word also used by Aristotle for the unfertilized egg of birds. The Soncono edition translated *ruah* as "inflated object" (Nid. 9b), but I feel that the modern term "blighted egg" probably comes closest to the original meaning.

Although the literature of the surrounding peoples gives ample evidence that artificial interruption of pregnancy was an everyday practice, as evidenced by Aristotle, Soranus, Ovid, Seneca, and others (Jakobovits), no mention is made of it either in the Bible or in the Talmud. Surely, if such practice would have been known either to Moses or the High Priests, its prohibition would have been included in the judicial code. But evidently, neither therapeutic nor criminal abortion was familiar to the ancient Jews, and therefore it did not present a problem that necessitated legislation.

Embryotomy. A different situation prevailed with regards to embryotomy. We read in the Mishnah: "If a woman is in hard travail, one cuts up the child in her womb and brings it forth member by member, because *her* life comes before that of the child; but if the greater part has proceeded forth, one may not touch it, for one may not set aside one person's life for that of another" (Ohol. 7:6). Unquestionably this precept refers to the living fetus, else the Mishnah would not talk of "the life of the child." That this law concerned the destruction of a full-term fetus and not, as Jakobovits argued, a therapeutic abortion is inferred from two facts: first, the text uses the expression *mekashah leyeled* (hard travail), the same expression employed in the description of Rachel's delivery (*vide supra*), and second, the Gemara takes great pain to explain "that the law relating to protracted labor does not apply to miscarriages" (Nid. 66a).

There is a slight variance in the interpretation of the text. The Mishnah specifies that one may not touch the fetus if "the greater part of its body has proceeded forth"; however, the Tosefta, a Mishnaic exegesis from the school of Rabbi Akiba, prohibited embryotomy, if the head was delivered (Yeb. IX, 4). This corresponds to

our way of thinking; once the head of a baby has been delivered, the rest of the body usually does not offer any difficulties, and therefore, embryotomy may hardly ever become necessary. Vice versa, in case of a breech presentation, the larger part of the baby may have been brought forth, whereas the delivery of the head may offer a major obstacle. In this latter case, the baby will die after several minutes because of compression of the cord, and thus embryotomy would be practiced on a dead fetus.

As Preuss pointed out correctly, these rules were not of an obstetrical but of a judicial character; thus they held the physician performing the operation as well as the patient exempt from penalty. The Talmud, therefore, has to look for a moral justification of the act. An opinion that might appear strange to the modern reader is advanced by Rabbi Huna: "A minor in pursuit may be slain to save the pursued" (Sanh. 72b). In other words, the fetus was regarded as a "pursuer" making an attempt on the mother's life and he thus had forfeited his protection under the law. But again, it is said that this status existed only as long as the head was not born. If the head was delivered, but the trunk failed to come forth (e.g., because of a shoulder dystocia), the mother was regarded as "pursued by heaven," i.e., an act of God, and embryotomy was forbidden. Preuss hastened to add that this view was disregarded by later Talmudic scholars.

CESAREAN SECTION

Besides embryotomy, there are two obstetrical operations that are mentioned in both parts of the Talmud and have caused a great deal of confusion and controversy: *keriyath habeten*, which connotes the opening of the abdomen after the death of a gravida to extract the child, and *yotze dofen*, which is translated in the Soncino edition as cesarean section, although Goldschmidt's translation *Seitengeburt* is somewhat less committal. Both methods of delivery had in common that the child thus brought forth was not a *peter rechem* (opener of the womb). According to the Bible, only a baby that "opened his mother's womb," and therefore was born through the vagina, merited the title *bekhor* (first-born) and thus was entitled to a *pidyon haben* (redemption of the first-born) (Exod. 13:13), as well as a double share of his father's inheritance (Deut. 21:17). Consequently, children born in any other way were not entitled to this privilege. What distinguished both births was that after a *yotze dofen* the mother survived, whereas *keriyath habeten* was performed only on a dead woman. Therefore, this term may be best translated as "post-mortem cesarean section."

Keriyath Habeten. This operation has been known for many centuries. It was first commanded by the Roman King Numa Pompilius (715–673 B.C.E.) in his *Lex Regia*. According to this law, no pregnant woman dying during the last month of pregnancy was to be buried without having her baby delivered through an abdominal incision. The Talmud takes up this question when discussing the management of executing a pregnant woman. On that occasion, Rabbi Nahman said in the name of Mar Samuel: "If a woman who has been sitting on a birthstool died on a Sabbath, one may bring a knife and cut her womb (*keresa*) open to take out the child" (Arak. 7a). However, the fetal salvage must have been small, just as it is today: out of

three attempts of post-mortem cesarean section, I have never been able to obtain a living child, for when a gravida is *in extremis* the oxygen gradient becomes so low that the baby will first suffer from hypoxia and later from a complete anoxia causing its intrauterine death. The sages gave a somewhat more poetic explanation of the fetal wastage: "The child's life is very frail. A drop of poison from the angel of death enters and destroys its vital organs" (*loc. cit.*). The order to perform a post-mortem section is so much more remarkable because Mosaic law declares that anybody who touched a corpse was unclean for seven days and therefore prohibited it (Num. 19:11). But here again, the attempt to save the baby's life superseded all other religious precepts and even permitted desecration of the Sabbath.

Yotze Dofen. The term cesarean section or Latin *sectio caesarea* has its origin in Pliny, who wrote in his *Historia Naturalis*: "*Auspicatus enecta parente gignuntur, sicut Scipio Africanus prior natus primusque Caesarum a caeso matris utero dictus, qua de causa et Caesares appellati*" (VII, 9, cited after Martius and Ramsauer). Thus, Pliny implied that the name Caesar came from the Latin *caedere*, "to cut," so that *caesus* would mean "one who has been cut out." Findley pointed out correctly that nowhere in the ancient Greek or Roman literature is any mention made of a cesarean section on a living woman, thus the only possibility could have been that Caesar was "cut out" from the belly of his dead mother. This is inaccurate, for we know that his mother survived his birth. Therefore, one has to surmise that the term cesarean section was derived from the *Lex Regia*, which later became known as *lex caesarea*, and from this law the name cesarean was derived (Findley).

Neither Hippocrates, Galen, nor Soranus knew of cesarean section on a living woman. According to Findley, it likewise was unknown in old Egypt. Thus, the Talmud is the only writing of antiquity that tells about such an operation. Semantically seen, the term *yotze dofen* in modern Hebrew means only that something "deviates from the normal" or is "abnormal" (Israeli). According to the supplement to Kaufman's English-Hebrew dictionary, the modern translation for cesarean section is *ledath hetekh* or *hitukh dofen*. As Preuss pointed out, nowhere in the Talmud is there any detailed description of the operation, and he concluded that it must have been general knowledge, which made a detailed description superfluous. The first authentic use of the term *sectio caesarea* is found in the writings of the Jesuit Father Theophilus Raynandus, who in 1637 published a treatise in Lyon, France, entitled: "*Tractatio de ortu infantium contra naturam per sectionem caesaream*" (Martius and Ramsauer).

The literal translation of *yotze dofen*, "brought forth through the side" (side-birth), leaves the mechanics of the operation to the imagination of the reader. Goldschmidt, the famous German scholar and translator, remarked: "Considered linguistically as well as in its context, *yotze dofen* or *derekh dofen* is not a normal birth but one coming forth from the side (dofen means 'side-wall' or 'rib'). Like many other cases, it is discussed theoretically in the Talmud and it later even mentions menstrual blood coming from the side [Nid. 41b], and all that has been written about the talmudists' knowledge of cesarean section is idle, silly talk (*eitel Faselei*). The explanation of Rashi [Hul. 51b]: through a *sam* ('medicament, drug') thus not through operation, only proves that he neither knew the cesarean section" (vol.

XII, p. 424, footnote 125). Thus, Goldschmidt's opinion on this subject is unequivocally in the negative. The *Encyclopedia Judaica* comes to the same conclusion (vol. VII, p. 147): "Whether a cesarean section on a living woman was performed in Talmudic times is doubtful."

The Talmud mentions the *yotze dofen* in two connections: first, as performed on animals and, second, when done on a human being. An animal delivered by cesarean section is not equal to those born normally, as shown by a quote that declares them unfit for the religious sacrifice (Zeb. 84a). In the *masekhta* dealing with the firstling's right, it is brought out that the law of the firstling is invalid in animals extracted through cesarean section (Bek. 19a). Their inferiority is further documented by the rule that not even the infant "following that born by *yotze dofen* is either a first-born for inheritance nor a first-born to be redeemed from a priest" (Bek. 47b). In a later ruling their inferiority was believed to be so marked that they were likened to "an animal which covered a woman or an animal that was covered by a man, or an animal set aside or used for idolatry, or a harlot's hire" (Tem. 28a). These citations give ample proof that the value of such an animal delivered through an abdominal incision was exceedingly low. The Talmud does not make it known whether the dam survived after such propagation or not, which distinguishes this operation from the *yotze dofen* on a human being, where it is assumed that the mother remained alive.

The last-mentioned topic takes up two entire folios of the *masekhta* Nidda, particularly with regard to the question of uncleanness after a *yotze dofen*. According to the majority of the rabbis (only Rabbi Simeon took exception) it was not considered a valid birth, and therefore, the woman did not have to observe the same number of days of uncleanness as after a vaginal delivery (Nid. 40a). As mentioned before, the Talmud reports on a twin pregnancy where the *sandal* was delivered through the birth canal, whereas the living fetus was extracted by *yotze dofen*.

One reason advanced for the unlikeliness of the knowledge of cesarean section was that anesthesia was supposedly unknown. However, as Boaz Cohen pointed out, an example is cited in the Talmud where an arm was to be amputated either by a knife or by a *sam* (drug), and Rashi remarked that this drug probably had some kind of anesthetic quality (Bab. Kam. 85a). Another interesting reference was a story reported of Rabbi Eleazar who apparently suffered from lipomatosis: "Thereupon he was given a sleeping draught, taken into a marble chamber [operating theater?], and had his abdomen opened, and a basketful of fat removed" (Bab. Mets. 83b). These quotations allow the conclusion that some form of anesthesia must have been known.

Anyone who has ever performed a cesarean section himself will agree that bleeding sometimes is a quite formidable problem and, according to Findley, was one of the main obstacles to this operation in the Middle Ages. These women died either from hemorrhage or infection, and although there have been a few isolated cases of cesarean section reported in those years, it never gained any popularity with the medieval surgeons. One should not forget that it was uncommon to sew incisions, but one poured some form of wine over the wound to effect hemostasis; moreover, massage of the uterus was said to have stopped the bleeding. In only one instance has it

been reported that an abdominal wound was sutured. A Roman who evidently was not a physician once saw a man fall from a roof so that his abdomen ruptured and he eviscerated. When the man fainted, his tense abdominal muscles relaxed, whereupon the Roman sewed him up (Hul. 56b).

Even Maimonides, who besides being a rabbi was likewise court physician of the Sultan Saladin, did not believe that a cesarean section such as we understand it today was ever done in Talmudic times. The *Jüdisches Lexikon*, a Jewish encyclopedia written in German, reported that by *yotze dofen* was meant a laparotomy for an abdominal pregnancy (vol. IV, p. 22), which is more plausible. It is hard to believe that the incidence of abdominal pregnancies, which today ranges at about 1 in 15,000 deliveries (Eastman), was so much greater in Talmudic times as to justify the creation of special rules regarding this condition, but it is the only obstetrical situation where an operation similar to a *yotze dofen* would have been possible. A simple laparotomy may have been within the scope of procedures practicable with the limited means at the disposal of physicians of that era. It could have been carried out with very little bleeding and may have healed without suturing the abdominal walls. It can be surmised that the placenta, whose removal often leads to uncontrollable hemorrhage, was left in place, thus avoiding this danger. But that by *yotze dofen* was meant an incision into the myometrium, either cervical or corporeal, is highly improbable. It may, therefore, be more appropriate to translate the Hebrew term as "abdominal delivery" rather than the now usual "cesarean section."

When reading Biblical or post-Bibilical literature, one often does not have the right to take all facts given at face value, but one should see them in the light of the state of medical science at that time. The Talmudic sages often employed a trick whenever they wanted to prove a point: they conjured up fantastic stories that they themselves did not believe and injected them into the debate. Preuss gave a lucid example concerning discussion of the rights of the firstling: "What if a weasel inserted its head into the womb and took the fetus into its mouth and thus extracted it? You ask 'And thus extracted it?' Render thus: What if the weasel took the fetus into its mouth, extracted it thus, inserted its head again into the womb and spewed out therein, and then the fetus came forth of its own? What is the law if one joined two wombs of two animals to each other and the fetus issued from the one womb and entered the other? Shall we say that it exempt only its own dam from the law of the firstling but it does not exempt another animal?" (Hul. 70a).

It appears to this writer that the rabbis had no clear understanding of the exact procedure of a cesarean section; the only thing they knew was that the baby did not come out from the vaginal orifice, and the woman had an incision in her abdomen. Thus, it is most probable that *yotze dofen* meant a laparotomy for an abdominal pregnancy. But, as Boaz Cohen remarked: "The last word on this problem of *yotze dofen*, medically speaking, has not yet been said."

THE FLAME AND THE LIGHT*

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The flame and its light.

The flame—light and warmth, clarity and passion—is perhaps the best symbol for the spirit of scientific research. To Heraclitus of Ephesus, the flame portrayed *change*, for him the only reality, since only change is eternal, *panta rhei*. But the flame also symbolizes the spirit of the investigator, whose impassioned search for the truth drives him to dedicate his whole life to pursuing that moment of light that, although often is as unattainable as the light of the stars, will illumine him with its radiance.

From time immemorial the investigator has conducted his quest by the light of a flame. In Paris, Vesalius performed dissections by candlelight; Cajal in Madrid toiled in a cellar lit by a taper; in Berlin, Ehrlich's head was forever bent close to his laboratory burner. Today, physics researchers sometimes work by the Dantesque glare of a hydrogen flame.

MD in the February issue presents the dazzling panorama of scientific research, old and new, including its philosophical aspects; the difference between invention and discovery and between basic and applied scientific research; the role of luck, design, and intuition in scientific discovery; and the history of scientific research and its present grandiose landscape with its brilliant teams of men, often working in vast laboratories with extraordinary tools and machines. Nothing defines better the creed of scientific research than the Second Charter (1663) of the Royal Society of London: "To further promote by the authority of experiment the sciences of natural things and of useful arts, to the glory of God the Creator, and the advantage of the human race."

Here I should like to concentrate on the inner flame that burns within the investigator himself, on his spiritual resources and his capital virtues, which not so long ago I described as seven in an address on that admired and beloved investigator Carlos Finlay, "the Pasteur of the Americas." Those seven virtues are present to a varying degree in every investigator, be he a Nobel Prize laureate or one of those even more admirable scientists—the general practitioner, the unnamed surgeon, the obscure laboratory worker—to whom research means abnegation and self-sacrifice.

History, including that of medicine, is made by men, and the number of spiritual carats such men possess determines the scope and magnitude of their achievements. For even in the sober, austere, impersonal climate of science, besides purpose and method, spirit also is required. This spirit is provided by the men who are making science today.

Benjamin Franklin once said: "All mankind is divided into three classes: those

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that are immovable, those that are movable, and those that move." Scientific investigators belong to "those that move." They do things. They express their greatness in actions of vast consequence to mankind. On their virtues depends the progress of science. The best scientific machine or instrument, the most perfect laboratory, the most advanced statistical methodology, the latest electronic advances, all these would be worth nothing without the men who, in the laboratory, clinic, office, or library, contribute their lifetime so that the stately chariot of medicine may move forward. Without these men no history of medicine could be made, just as without pillars to support its foundations no good building could be erected.

Foremost among the investigator's virtues I place *goodness*. A castle is as strong as its foundations. Every great man, every great investigator, begins by being a good man. The humaneness of daily life must overflow into the humanism of the investigative genius. In no profession as in medicine is it so important to be a good man. "Science without conscience is nothing but baseness of the soul," said that lapidary of eternal truths, Montaigne. The true investigator is an indefatigable galley slave of medicine, who, renouncing the glitter of easy success and tempting profit, chooses the troubled seas of investigation instead of the calm harbors. Modesty is usually the inseparable companion of such goodness.

The second quality is *greatness*. Greatness is simplicity. This has been so from Hippocrates to Fleming. A greatness that is an aristocracy of the spirit is the only sovereignty people can accept without relinquishing their own sovereignty. Greatness in the true investigator means to go through life doing with a simple spirit those things that may benefit his fellow beings, building a mighty pyramid without losing his childlike innocence of soul. It is to remain indifferent in the face of indifference, to have faith in his convictions, even during the interminable night of failure, certain that the dawn will come. It is to accept life—as did El Greco in Toledo—as splendor and radiance, lighting the shadows of his laboratory with his own inner light.

Sometimes *genius* is added to these qualities. While in art knowledge is spasmodic and nonaccumulative, in science it is systematically accumulative and keeps on replacing itself. A Botticelli, a Cervantes, a Beethoven, each in himself is a complete cycle and therefore needs no predecessors and leaves no school. This is why a work of art—symphony, statue, painting—is immortal, while the life of a scientific work —report, address, lecture, or research data—is ephemeral and always liable to be superseded by more recent work.

In art, genius is the rebel artist who creates his own universe in its entirety; in science, genius is the rebel investigator who excels his universe by applying the spark of his intuition to already existing knowledge. Genius is intuition, but it is also logic in the service of a fervent vocation, displayed at the right time and in the proper place. Besides quality, genius is also quantity, as borne out by the prolific work of Paracelsus, Harvey, Hunter, Freud, and Fleming. The true genius rarely makes a single discovery. The great investigator, generally, makes many.

Add to that the *spirit of inquiry*, in which experimentation is the indispensable complement to theorizing and not a means for exploding sensational intellectual fireworks. Patience in waiting and quickness in thought distinguish the investi-

gator. Often the genius' intuition flashes suddenly, but the true investigator will, if necessary, spend years in verifying his spark of truth, reconciling noble haste—haste, eternal companion of the creator—in his endeavor, with patience in its confirmation. William Harvey did it and so did Theobald Smith.

Lucidity is another quality indispensable in the investigator, because the style is the man, or in other words, man in his human quality is his style. In his tribute to Claude Bernard, delivered in Paris on April 3, 1879, the great historian Ernest Renan said of Bernard's style what could be applied today to any investigator: "Human intelligence is a whole so well united in all its parts that a great mind is always a good writer. The true methods of investigation, given a firm and healthy judgment, embrace the solid qualities of style. . . . The standard of good scientific style is lucidity, perfect adaptation to the theme, complete forgetfulness of self, absolute abnegation. That is also the standard for writing well, whatever the subject. The best writer is the one who develops a great subject and forgets himself in order to allow his subject to speak for itself. . . . He uses words like a modest man uses his clothing, to cover himself. . . . He thinks, he feels, the words flow. . . ."

The style of the good investigator sparkles with the diamantine brilliance and limpidity typical of the man who knows certain things thoroughly and wishes to explain them so that everyone will understand. Reading great writers, like Erasmus and Juan Luis Vives, one realizes that style is like the acrobat's tights, which cover his figure without concealing it. Style is a close-fitting glove on the hand of thought. Fleming's reports are like a transparent window through which one can see unmarred by a single mote of dust the wide prairies of his thought. The creed of the true investigator is fidelity to the truth, and that means not only to seek it and serve it, but also to express it in language intelligible to everyone. Finlay, Cajal, Freud, Fleming, Osler—these men allowed no hyperbole or redundancy, no exaggeration of concepts, to creep into their prose and cripple its scientific probity. Lucidity in style presupposes lucidity in thought, and this in turn implies clarity of spirit. A clear style, like a clean windowpane, indicates that the owner does not fear inquisitive eyes. The investigator's prose must be fluid, fresh, and crystalline, like water from a mountain brook.

The investigator is also a true *patriot*, for he is a living part of the historical conscience of his epoch. He can look at the problems of his country and of his time with eyes both critical and loving, for the true lover does not respond blindly to Cupid's darts but loves his beloved though his eyes are wide open to her defects. The investigator's homeland grows with each of his discoveries, until it becomes a universal homeland not to be found in any geography book. The investigator is the *homo universalis* of our time and helps to promote the health of all people on our planet. He can sometimes, without leaving his home or country, delve so deeply that he reaches universal roots, preferring vertical profundity to horizontal spread, which guarantees his universality in space and his immortality in time.

Finally, the investigator possesses *universality*. In the address already quoted, Renan said: "Glory has something homogenous and identical. Everything that vibrates produces it. There are not various types of fame, any more than there are various kinds of light." All types of glory derive their rays from the same source. The in-

vestigator's glory is universal and clothes with honor all who admire an ideal and dedicate themselves selflessly to it.

These seven virtues inspire one with absolute confidence in the future of science. Medicine must become more and more scientific and at the same time more humane and humanistic, making of technology a servant and not a tyrant, using the machine as an aid to the investigator.

Atomic physics is struggling valiantly to conquer outer space; medical research must struggle equally to conquer the inner space of man himself. On a better knowledge of man's physiological inner space depends the improvement of his health; on a better knowledge of his psychic inner space depends the improvement of his mental health and of the health and peace of nations.

Perhaps in order to progress in this fascinating exploration of man's psychic inner space, the scientific investigator should ask himself the same portentous questions asked 2500 years ago by the philosopher-physicians of ancient Greece: What is man? What is his destiny? What is his place in the universe? Having asked those three formidable queries, on which was founded the historical development of man's dignity, the investigator may find the answers in the flame—light and warmth, clarity and passion—of his seven spiritual virtues.

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The Historical Development of Physiological Thought. A Symposium at the State University of New York Downstate Medical Center. EDITED BY CHANDLER MC C. BROOKS AND PAUL F. CRANEFIELD. The Hafner Publishing Company, New York, 1959. Pp. 401. $6.00.

To commemorate the one hundredth anniversary of the founding of the Downstate Medical Center of the State University of New York, a series of symposia were held at the university devoted to the study of "how knowledge is obtained; how, in the past, basic medical science acquired the concepts and intellectual procedures which are now automatically followed." Physiological concepts were chosen as the best examples of how we have reached our current knowledge and "understanding of the operation of biological systems and the behavior of living organisms."

The first section of the book, dealing with "Medicine and Basic Scientific Thought," includes an admirable study of Owsei Temkin on "The Dependence of Medicine upon Basic Scientific Thought," in which we find a passionate plea for physicians to read not only history and biography, but also good literature to enhance their ability to better understand patients. The author quotes Sydenham's advice to a medical student who inquired what to read to qualify him for practice: "Read *Don Quixote*, it is a very good book, I read it still."

In the second section devoted to "The Basis of Integrative Function and Human Behavior," that is, to the principles of the function of the central nervous system and the brain, Lloyd G. Stevenson, in a splendid paper on "Anatomical Reasoning in Physiological Thought," emphasizes the basic role of anatomy in the development of physiology, reminding us that William Harvey, physiologist *par excellence*, was considered in his own age an anatomist, and that to Jean Fernel, the humanist, the value of anatomy lay in its giving the "geographical" setting of events.

Another paper in this section, "The Development of Ideas on the Synapse," by Sir John Eccles, first explains clearly the contributions made by Cajal, Sherrington, Dale, and others, and then brilliantly presents the electron microscopy of the synapse and the problems that remain unsolved.

To the late John F. Fulton was assigned the "Historical Reflections of the Backgrounds of Neurophysiology," and his paper, which includes some deeply perceptive highlights on Sherrington, Descartes, Digby, Setchenov, and Pavlov, together with the social implications of mass conditioning in man, is one more great demonstration of the vast knowledge of medical history and science of the beloved master.

A great anatomist, Horace W. Magoun, traces with exceptional erudition the "Development of Ideas Relating the Mind with the Brain," from Platonic biology to Vesalius.

Homer W. Smith, speaking about "The Biology of Consciousness," delves at length with unusual perceptiveness into the concepts of "an obscure and somewhat peculiar Frenchman, living at the time (1637) in Holland," and elegantly relates Descartes' philosophical concepts to our present knowledge of consciousness.

In his "Development of the Concept of the Dynamic Process in Psychiatry," the distinguished author, Gregory Zilboorg, sets up a brightly lit stage of medical history, upon which with lively words he brings back to life again the figures of Paracelsus, Weyer, Broussais, Holmes, Freud, and others who contributed so much to establish the dynamic nature of human psychology.

In the third section on "Humoral Transport and Integrative Function," the outstanding pharmacologist, Chauncey D. Leake, brilliantly presents "The Development of Knowledge About the Cardiovascular System," adopting Harvey's achievements as the center of a vast historical cavalcade, in which Harvey's predecessors and successors are given due recognition.

Starting with the Galenic concept of humors flowing in tubular nerve trunks, and ending with the current concepts of chemical mediation, Chandler McC. Brooks, in his erudite paper, "Discovery of the Function of Chemical Mediators in the Transmission of Excitation and Inhibition to Effector Tissues," excellently presents the humoral and chemical mediation of neural action. There is another paper by this same author and Harold A. Levey entitled "Humorally-Transported Integrators of Body Function and the Development of Endocrinology," which we consider an extraordinary work. It sums up in a most lucid way all of our knowledge of this subject, and it is a great historical contribution to the history of endocrinology.

"Mechanistic Thought, Energetics, and Control Theory in Biology" occupies the fourth section of this book, and in it the greatest historian of public health, George Rosen, presents in his usual lively and profound style, "The Conservation of Energy and the Study of Metabolism." This brilliant paper starts with the famous letter written by Alfred Russell Wallace to his friend Charles Darwin on the book *Progress and Poverty*, by Henry George, in which occurs an argument on the conservation of energy, and ends with a brilliant dissertation on contemporary studies on intermediary metabolism.

In the same section, Ludwig von Bertalanffy presents with clarity and vigor the "Modern Concepts on Biological Adaptation," starting with a passage from Plato's Symposium, in which such concepts were already outlined, and leading to the relationship between body and mind.

In the final section of the book, "The Vital Process and the Disease State," Iago Galdston makes use of his encyclopedic knowledge to explore the problem of "Physiology and the Recurrent Problem of Vitalism," beginning at the very moment when Friedrich Wöhler synthesized urea and ending with the concepts of Nicolai Hartmann reconciling purpose, teleology, and freedom in biology.

"What Keeps Men Alive?" is the subject of a learned and convincing dissertation by Bruno Kisch on the history of thoughts about life and death.

This book ends with an extremely interesting study on "The Contribution of Pharmacodynamics and Pharmacology to Basic Physiological Thought," by as distinguished an authority as Alfred Gilman, and with a paper on "Towards a Philosophical Study of the Idea of Disease" in which the author, L. J. Rather, most aptly reviews the idea of disease as an entity, from the *Timaeus* to the present time.

If we have delved at length on the contents of this book, it is because of its sustained excellency, which applies equally to all its articles, and because it is a brilliant

example of how historical symposia should be conducted and good editing should be done.—*Félix Martí-Ibáñez, M.D.*

Chemical Quantitation of Epinephrine and Norepinephrine in Plasma: A Clinical and Experimental Study: A Study of Epinephrine and Norepinephrine: Their Plasma Concentration in Hypertension, Shock, and Mental Disease, With Some Metabolic Studies. WILLIAM MUIR MANGER, KHALIL G. WAKIM, AND JESSE L. BOLLMAN. Springfield, Ill., Charles C Thomas, 1959. Pp. 398. Price $11.50.

In this book is described a modification of a fluorescent technique for chemically quantitating epinephrine and norepinephrine in plasma, pheochromocytomas, and cerebrospinal fluid. Experimental and clinical studies are reported illustrating the value of this method as a diagnostic aid and to increase our understanding of some of the physiochemical derangements that occur in various forms of stress and of the metabolism of epinephrine and norepinephrine.

Further studies are needed to assess the value of this new fluorescent method as a clinical and research tool.

Books in Brief

Space Biology: The Human Factors in Space Flight. JAMES STEPHEN HANRAHAN AND DAVID BUSHNELL. New York, Basic Books, Inc., 1960. Pp. 263. Price $6.00.

This is a fascinating survey of the history of man's interest in space flight and the recent outstanding developments that have made it possible. Experiments are described illustrating the problems of biological adjustment to space flight, problems created by acceleration, weightlessness, radiation hazards, waste disposal, maintenance of food supply. Although technical, the discussion, supplemented by an impressive bibliography, is lucid, enlightening, and interesting.

The Seven Ages of Woman. ELIZABETH PARKER, M.D. Baltimore, The Johns Hopkins Press, 1960. Pp. 609. Price $6.50.

A sympathetic discussion of the physical, psychological, and spiritual development of woman through the seven stages of her life—age of the unborn, of infancy and childhood, of youth, of maturity, of marriage and motherhood, of the menopause, and of serenity. A book of value for every woman seeking the answers to the "mystery of femininity."

Cold Injury: Transactions of the Sixth Conference, July 6, 7, 8, 9, and 10, 1958, U. S. Army Medical Research Laboratory, Fort Knox, Ky. New York, Josiah Macy, Jr. Foundation, 1960. Pp. 375. Price $6.50.

Proceedings of a very interesting conference on cold injury, including reports of medical experiences at the South Polar ice cap, studies of hibernation in mammals, field studies on cold adaptation, and other reports. Many of the problems discussed have not been studied previously.

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A HISTORY *OF* NEUROLOGY

by Walther Riese, M.D.

Associate Professor of Psychiatry and Neurology; Chairman, Department of the History of Medicine, Medical College of Virginia, Richmond, Virginia
Consulting Neuropathologist to the Department of Mental Hygiene and Hospitals of the Commonwealth of Virginia

Here is a new approach to the history of neurology. With an historian's eye for the dynamic, the author has chosen to focus on "the great and lasting problems" that have remained inherent in man's endeavor through the ages to understand the functions of the nervous system and their disturbances. By concentrating on fact, thought, and theory, Dr. Riese has achieved a comprehensive picture of neurologic progress.

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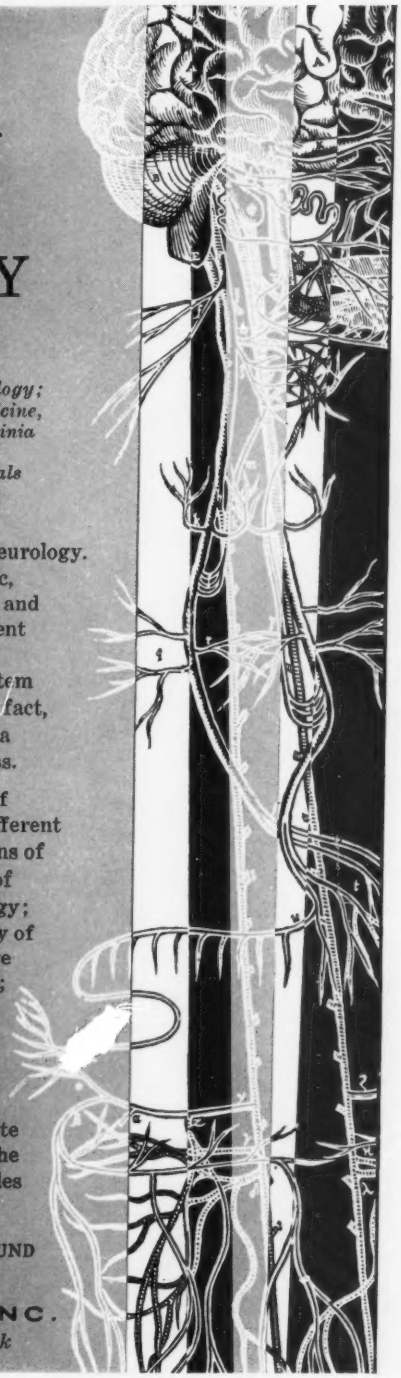

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A New MD Medical History...

A HISTORY *of* OPHTHALMOLOGY

by George E. Arrington, Jr., M.D.

Associate in Ophthalmology, Medical College of Virginia, Richmond, Virginia

A HISTORY OF OPHTHALMOLOGY provides an over-all view of ophthalmological progress through the ages. With scholarship and originality the author traces the thinking, of men known and unknown, that has made possible the technological advances of this science. Man's search for understanding of vision and its preservation is shown effectively in its relation to the history of civilization. The content of this book ranges from the period of prehistorical ophthalmology to the present day. In emphasizing the effect of related sciences, philosophy, and human culture upon ophthalmology, Dr. Arrington offers new insight into his subject. Appropriate attention is given the ascendancy of modern ophthalmology including an evaluation of its current trends in the light of the future. It is a book of interest to ophthalmologists, general practitioners, and students.

This volume is one of a series devoted to the histories of various specialties and facets of medicine. Félix Martí-Ibáñez, M.D., who wrote the foreword to A HISTORY OF OPHTHALMOLOGY, is the Editorial Director of the series, which includes books on Public Health and Neurology.

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